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THE COVER

This is the hand of a man with pellagra. It is as if he were reaching or even begging for the abundance of food in the top right corner. This cover therefore symbolizes the nutritional problems of the world of today.

The mal-distribution of food is of course a social, not a medical problem. On the other hand, by stressing and teaching balanced diets, the profession can greatly decrease the incidence of deficiency diseases. By understanding the physiology of nutrition and the composition of foods, we are capable of intelligent treatment of disorders as they arise.

J. L. M.

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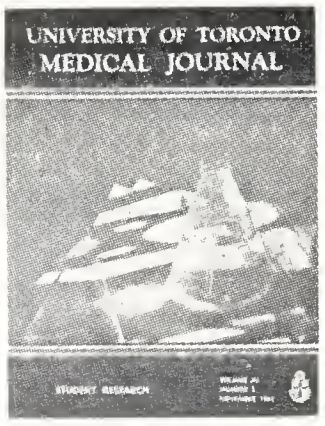

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Editorials

NUTRITION IN MEDICINE

As early as 25 B.C. Celcus emphasized the role of foods in maintaining health when he stated, "Food and drink nourish and are of general assistance not only in diseases of all kinds but in preserving health as well". The role of foods in the treatment of disease was later introduced; scurvy was the first example. In the 16th century Clowes described the cure of two seafaring men who fell sick at the Sea of Scorby using a remedy "cochleria or scorby grass". In the next century Venette recorded the usefulness of vegetables and fresh fruits as antiscorbutics. In 1734 Bachstrom recognized scurvy as a deficiency disease. Today many diseases which are caused by a lack of certain nutrients are recognized.

As our way of life has changed due to improved communications, transportation and new developments of industry, we have less need to worry about lack of nutrients but more cause to be concerned with excesses. In this connection overweight in most cases is due to a greater intake of food than is necessary to supply the energy required for our type of living. In short, we eat too much of all kinds of food. For each pound of fat that is added to our frame, it is believed that the body adds one mile of blood vessels to supply nutrients to these fat cells. For every ten pounds of extra fat there are ten miles of extra blood vessels. Obviously this load increases the work of the heart. Is it any wonder that the incidence of cardiovascular diseases is higher in obese adults than in normal weight men and women? Vital statistics for the past thirty years bear out this fact

What is the ideal weight of a man with average-sized bones and muscles? During the Second World War, Behnke, using Navy personnel, determined their "lean body mass" i.e. bones and muscle. The average weight per inch of height was found to be 1.8 pounds. Using a method to determine specific gravity he was able to calculate the normal amount of fat in relation to the weight of the bones and muscle. From these data he showed that the body should contain 10 to 15 percent fat. Using this scheme the ideal weight of a six foot man should be $72 \times 2 = 144 + 15\%$ or 165 pounds. In many cases this value coincides with the individual's weight at 25 years of age. It would appear then that middle age spread is not healthy! With women, who generally have smaller frames and less well developed muscles, a satisfactory rule of thumb for their ideal weight is less than two pounds per inch of height.

Recent epidemiological studies of Dahl, and animal experiments carried out by Meneely suggest that progressively larger intakes of sodium chloride may be a chronic factor in influencing the pathogenesis of hypertension. Numerous other studies on this disease have shown that moderate restriction of sodium intake is successful in lowering blood pressure. Evidence is also accumulating which indicates that the use of a well balanced diet, along with the curtailment of food in general, does accelerate weight loss. As excess fat is removed the extent of blood vessels is reduced and the work of the heart is decreased accordingly. Therefore, diet is an important factor in reducing the abnormally high blood pressure found in this disease.

With the current emphasis and dramatic advances through medical research it seems highly probable, in fact certain, that nutrition will assume an increasingly prominent role in the science of medicine and ancillary health fields.

Barbara A. McLaren, Director,
Faculty of Food Sciences.

A LIFE OF SERVICE

The fellowship of those who bear the mark of pain knows no boundaries. They belong together the world over.

So said Dr. Albert Schweitzer, a man who gave up European life to serve in a lonely corner of Africa. Half the people in the world are rarely, if ever, treated by a physician, and some areas have only one doctor for 200,000 people. Having one of the world's highest standards of living, we have a moral obligation to these medical indigents. Every doctor knows he must live a life of service, and perhaps some, forgetting personal interests more than most, will recognize their responsibilities outside North America.

Many groups promote medical service in Asia, Africa and Latin America. World Health Organization and Medico recruit doctors for overseas service. Medical personnel are accepted by Canadian University Service Overseas, and the African Students Foundation can direct doctors desiring work in Africa. The Student Christian Movement of Canada lists openings in mission hospitals. Opportunities are almost unlimited, but how many of us will act on our world-wide responsibilities to help ease the pain?

J.D.G.

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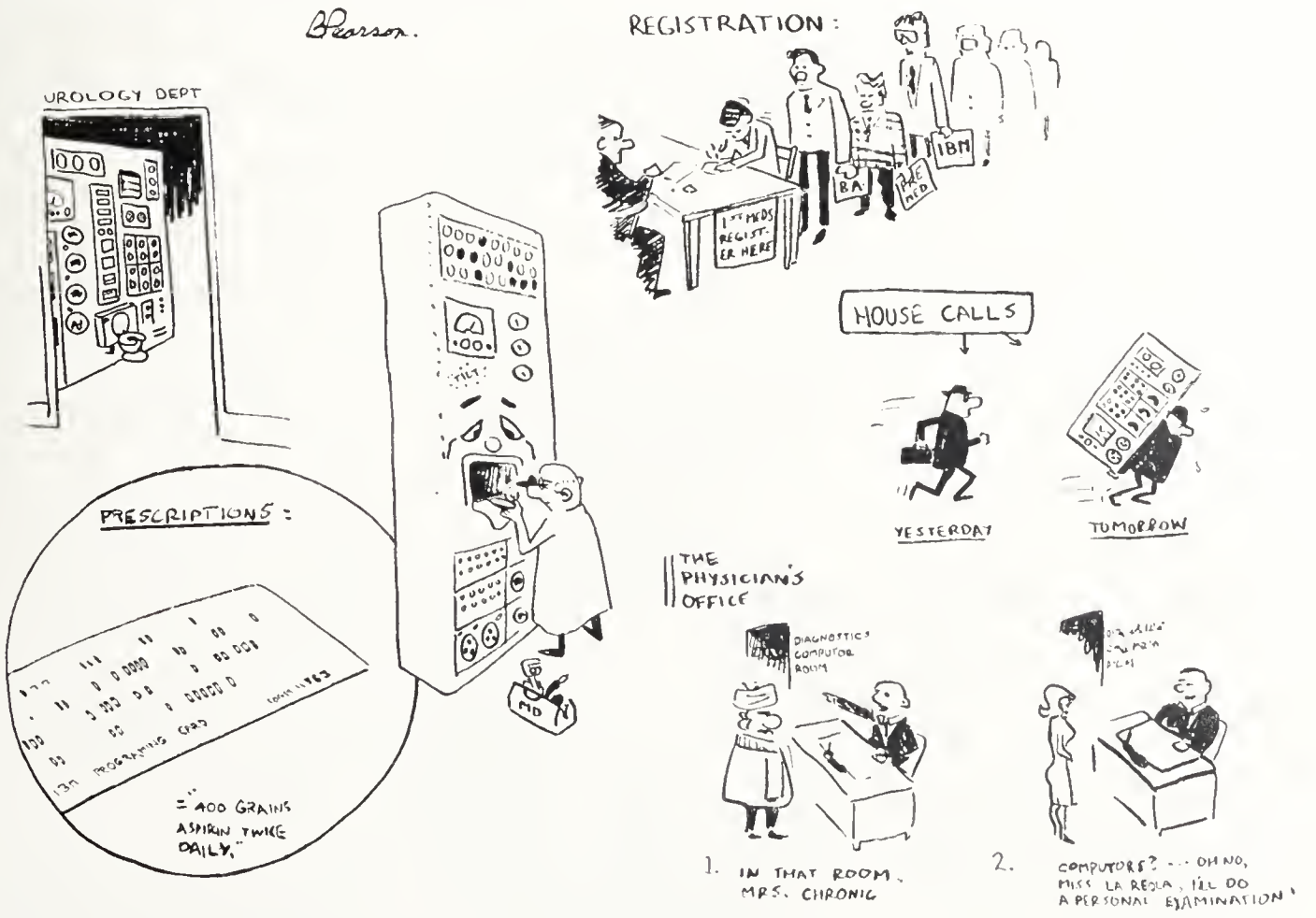

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The Essentials of Nutrition

J. L. Madigan 6T3

Presenting the elements of the normal diet, the author points out disease states associated with excesses or deficiencies of these elements, and finishes with an approved menu.

There are six types of nutrients present in some or all foods in variable proportions: carbohydrates, fats proteins, water, minerals and vitamins. The carbohydrates, fats and proteins that are not used for growth and repair provide calories. Thus we have the seventh factor.

The optimal supply of food is one which provides calories and all other nutrients in amounts sufficient to meet all the needs of the individual. Requirements for optional nutrition are influenced by age, sex, growth, exercise, climate and disease, as well as the relative proportions of nutrients in the diet. For instance, the thiamine requirement is increased in a high carbohydrate, low fat diet.

The body has a variable capacity to absorb, store, synthesize and eliminate substances according to their availability, need, and rate of use. For example, the liver contains approximately a thousand micrograms of cyanocobalamin. It can readily be seen with a requirement of one microgram a day, that the effects of a deficiency (pernicious anemia) would not be manifest for nearly three years. The normal kidney's ability to excrete excesses of water and electrolyte and to conserve the same in times of deficiency is well known.

Causes Of Deficiencies

1. Defective intake of food
   anorexia, chronic vomiting, alcohol, food fads, old age and unappealing preparation of foods plus economic problems.
2. Defective digestion and absorption
   steatorrhoea, dumping syndrome, antibiotics, infective diarrhoea.
3. Defective utilization
   cirrhosis, malignant disease, chronic disease, hyperparathyroidism.
4. Loss of nutrients from the body
   nephrotic syndrome, diabetes mellitus, diabetes insipidus, menorrhagia, bleeding ulcer, parasitic infestations.
5. Nutritional needs increased
   pregnancy, lactation, growth, exercise, fever, hyperthyroidism, burns, fractures, surgery.

Causes Of Exeesses

1. Habit
2. High (calorie) fat diets
3. Psychological
4. Extended use of large doses of vitamins
5. Eating certain foods such as polar bear liver

Thus it should be appreciated that nutritional disorders do not result from sporadic daily, dietary indiscretions, but rather from prolonged omissions or over-indulgence of one or more of the six types of nutrients.

THE CHIEF NUTRIENTS

Protein

Protein is one of the most important nutrients. In the child an ample supply is needed to insure adequate growth. The adult must have sufficient intake to replace tissue lost by normal wear and tear. Additional quantities are necessary after major operations, wasting illnesses, during pregnancy and lactation.

The breakdown of protein provides amino acids, eight of which are considered essential for an adequate diet. These are lysine, tryptophan, phenylalanine, leucine, iso-leucine, threonine methionine and valine. Although these are considered essential because they cannot be synthesized by the body, the amounts required of each are not absolute because of the ability of the body to make adjustments by partial synthesis, and replacement of sub-optimal amounts by non-essential amino acids. If there is a complete absence of one or more of the eight mentioned above, an obligatory negative nitrogen balance results.

The *biological value* of protein is based on the content of essential amino acids. Broadly speaking, animal proteins have a high, and plant proteins a low biological value. It is not important whether the essential amino acids are obtained from a single source or from a mixed diet.

Consumption of carbohydrates, fats and proteins stimulate increased metabolic activity resulting in increased heat production. This is termed the *specific dynamic action* of foods. In proteins this is approximately thirty percent. It is recommended that a high protein diet be accompanied by simultaneous increased consumption of fats and carbohydrates in order to raise the energy intake to compensate for the increased metabolism.

Inadequate protein intake may result in (1) im-

pairment of liver function and liver cell necrosis, (2) changes in plasma protein (albumin) levels with subsequent edema, (3) wasting of tissues, and (4) kwashiorkor.

Adults can be maintained on as low as 30, or as high as 300 grams per day. Since there is no relationship between activity and requirements it is convenient to express amounts as proportions of total calories. Protein should form 10 to 12 percent of a normal adult's total calories, pregnant and lactating women and children need 15 percent. Adequate essential amino acids are assured if one-third or more of the requirements come from animal sources.

Fat

Fat is important because of its high energy value. It is a vehicle for the fat soluble vitamins A, D, E, and K, and contains the essential linoleic and linolenic unsaturated fatty acids. Food is also made less bulky, more palatable, more appetizing and premature hunger is prevented by its fat content. The specific dynamic action of fat is four to five percent.

A high fat diet, especially of saturated fatty acids is said to predispose to high serum cholesterol levels which is associated with patients suffering from coronary thrombosis. Although the evidence is very persuading, it is not yet established that elevated serum cholesterol causes heart disease, nor is it certain that the two above mentioned fatty acids are essential to man.

Fat deficiency in itself does not result in disease, but skin changes have been noted in a few infants on low fat diets. The disorders seen are the result of defective absorption of the fat soluble vitamins, which are mentioned under that section in this article.

Fat should form 25 percent of the total caloric intake.

Carbohydrates

Carbohydrates are the least expensive of foods and tend to form a large proportion of the diet, especially in the lower income groups. A very small amount is needed to prevent ketosis and in practice is always exceeded. In a diet containing carbohydrate to supply energy much less protein is required for nitrogen equilibrium. This is known as their *Protein sparing action.* The specific dynamic action of carbohydrate is four to five percent.

A relative thiamine deficiency is seen with excessive intake of carbohydrate in one crop diets (rice) of the far eastern countries. Specific disease entities of carbohydrate intake are very rare.

No information is available regarding amounts of carbohydrates necessary, and in practice it is used to make up the recommended daily caloric intake after protein and fat requirements are met.

Calories

Calories are supplied only by carbohydrates, fats, and proteins and in the following amounts known as Atwater factors. One gram carbohydrate yields 4 Calories. One gram fat yields 9 Calories. One gram protein yields 4 Calories.

This energy is used for five purposes. (1) Basal Metabolism, heart-rate, muscle-tone, breathing and body-temperature are maintained. (2) Energy is provided for increased metabolism due to the specific dynamic action of foods. In mixed diets this is approximately ten percent of the BMR. (3) Daily activities such as sitting, standing or eating are able to be carried out, as well as (4) exercise or work. (5) Calories also provide the energy equivalent for tissue deposition in growth.

The body is able to adapt itself to different levels of caloric intake and to become stabilized at the lower or the higher level. It does this as a result of alterations of the energy expended in the above five mentioned purposes. Caloric excess results in overnutrition or obesity. Caloric deficiency results in subnutrition or starvation.

The daily recommendations vary widely among similar individuals in similar occupations. Men require 2500 to 3500 calories, depending on their activity. Women need 2000 to 3000 calories, depending on activity, but this value is increased in pregnancy and lactation. Children should have 50 calories per pound in the first year of life; from ages one to twelve the requirement is 1300 to 2500 depending on the weight of the child.

Water

Water is important for its capacity as a solvent and for the regulation of the body temperature. Complete deprivation of water results in death in a few days. After partial deprivation, the signs and symptoms of dehydration are noticed; among them thirst, skin inelasticity, reduced urine volume, increased serum electrolytes and increased BUN.

The causes of water depletion are lack of availability of water, dysphagia, unconsciousness, or apathy for example in an aged patient. Water excess is not seen in the healthy individual.

Minerals

The physiologically important elements are sodium, chlorine, phosphorous, calcium, sulphur, iron, iodine, potassium, cobalt, fluorine, magnesium, copper, manganese and zinc. Deficiencies and excesses arise in a number of clinical situations. However they are

seldom the result of malnutrition but are usually secondary effects of disease processes. These may occur in endocrine disorders, chronic diarrhoea, renal disorders and metabolic defects. The following are the most important as far as nutritional disorders due to malnutrition are concerned.

Calcium. The blood level of calcium depends on the amount absorbed, vitamin D intake, the activity of the parathyroid glands and the rate of calcium excretion. It is important as structural material in bones and teeth, in the regulation of excitability of nerves, in the normal action of the heart and the skeletal muscle and in clotting of blood. Disorders are discussed under vitamin D. Daily recommendations vary. Young children should have 0.5 grams, and adults 0.5 to 0.7 grams. Children 11 to 19 years need 1.0 to 1.2 grams, and women in pregnancy and lactation require 1.2 grams.

Phosphorous in sufficient amounts is provided by a diet adequate in calcium. It is important in the formation of bones and teeth in the structure of the cell, and as part of the buffering mechanism.

Iron. The body contains approximately 4.5 grams; 70 to 75 percent in the haemoglobin of the blood, five percent in the myoglobin of muscle and porphyrin catalysts, with the remaining 20 to 25 percent in storage. Approximately ten percent of the amount ingested is absorbed. Deficiency results in anemia, seen most frequently in menstruating women, pregnancy, lactation and in association with poor diets. Excesses result in hemochromatosis and hemosiderosis. Daily recommendations include 6 mg. for men, 6 to 12 mg. for children and 12 mg. for women, 15 mg. when they are pregnant.

Iodine is essential for the synthesis of tetra and triiodo thyronine. Deficiency results in simple colloid goitre. This does not occur here with the use of iodized salt.

Vitamins

Vitamins are organic chemical substances which the body requires in small amounts for normal metabolism and cannot synthesize itself. The fat soluble group includes Vitamins A, D, E and K. The water soluble group includes ascorbic acid (vitamin C), thiamine, nicotinic acid, riboflavin, pyridoxine, folic acid and cynocobalamin (all included in the vitamin B complex).

The water soluble vitamins (except for cyanocobalamin) are diffusible and examples of impaired absorption are not common. Also, these vitamins may be stored in amounts sufficient to prevent clinical manifestations of deficiency from four months to a year. Any excess is rapidly excreted in the urine, thereby preventing toxic effects from overdose. The fat soluble vitamins depend on fat and bile salts for absorption. Disorders are seen in such conditions as steatorrhoea and biliary obstruction. Their storage is sufficiently adequate to prevent signs of deficiency for a year or so. They are not excreted in the urine and toxic levels may accumulate with prolonged overdosage. Vitamin K, nicotinic acid, riboflavin and folic acid are synthesized in nutritionally important quantities by normal intestinal flora.

Vitamin A. The primary biochemical failure in deficiency is unknown, but it manifests itself by night blindness, xerophthalmia (dry eye), keratitis and conjunctivitis, and follicular keratosis. Excess results in hypervitaminosis A, a rare condition which may be encountered when polar bear liver is ingested. Daily recommendations are 3500 to 4000 international units.

Vitamin D aids in the absorption of calcium and phosphate from the intestine and promotes increased absorption of phosphate by the renal tubules. Vitamin D deficiencies go hand in hand with calcium deficiencies, as far as disease states are concerned. The deficiency diseases are rickets in children and osteomalacia in adults. Excesses result in hypervitaminosis D, characterized by hypercalcemia, constipation, vomiting, polyurea, renal damage, osteoporosis and metastatic calcification. The daily recommended dose of vitamin D for children and women in pregnancy and lactation is 400 international units.

Vitamin E has no established function in man.

Vitamin K is necessary for the formation of prothrombin in the liver. Absorption from the gut depends on bile salts and fat. Deficiency results in hypoprothrombinemia with a subsequent hemorrhagic tendency. Daily recommendations are unknown.

Ascorbic Acid (Vitamin C) is present in all body tissues and fluids and is necessary for connective tissue and blood cell formation. Deficiency results in scurvy. Daily recommendations vary. Children to ten years need 20 to 30 mg., and those over ten need 30 mg. Women in pregnancy and lactation require 50 mg. per day.

Thiamine as thiaminepyrophosphate is necessary in carbohydrate metabolism. Deficiency results in beriberi. Daily recommendations are 0.3 mg. per 1000 calories.

Nicotinic Acid. The amide of this acid is a component of the coenzymes, DPN and TPN, which play a vital role in metabolism. Deficiency results in pellagra. Daily recommendations are 0.5 mg. per 1000 calories.

Pyridoxine is important as in a decarboxylase and deaminase and seems to be intimately concerned with the metabolism of the central nervous system. Deficiencies are seen as epileptiform seizures in infants and children, along with hyperirritability and gastro-intestinal distress, while in adults seborrheic lesions, lymphopoenia and anemia may result. These may be associated with Isoniazid therapy for tuberculosis. Daily recommendations of pyridoxine are 2 mg. for adults and 0.2 to 0.5 mg. for infants and children.

Folic acid is important in the formation of blood cells. It is synthesized in important amounts in the intestine. Deficiency results in a macrocytic anemia. Daily recommendations are unknown.

Cyanocobalamin is important for the formation of blood cells and in the function of the nervous system. Deficiency, more correctly malabsorption due to lack of extrinsic factor, results in pernicious anemia. The daily requirement is 1 microgram.

SUMMARY

Adequate amounts of proteins, carbohydrates, fats, minerals and vitamins can be insured by planning meals following the recommendations approved by the Canadian Council on Nutrition, 1961.

Milk is an excellent source of calcium, riboflavin and protein. Children (up to about 11 years) need 2½ cups per day and adults should have 1½ cups per day. Adolescents and expectant and nursing mothers need 4 cups per day.

Fruit. Two servings of fruit or juice should be given daily, including a satisfactory source of vitamin C (ascorbic acid) such as oranges, tomatoes, vitaminized apple juice.

Vegetables are good sources of iron, vitamin A and B vitamins. One serving of potatoes and two servings of other vegetables, preferably yellow or green are sufficient for one day.

Bread and Cereals supply B vitamins, Bread (with butter or fortified margarine), and one serving of whole grain cereal are necessary in a daily menu.

Meat and Fish supply protein, iron and B vitamins. One serving of meat, fish or poultry should be given daily. Eggs, cheese, dried beans or peas, may be used in place of meat. In addition, eggs and cheese each at least three times a week are useful supplements. Liver should be eaten occasionally.

Vitamin D. 400 interntional units is necessary for all growing persons and expectant and nursing mothers.

Iodized Salt is one of the only dietary sources of iodine.

ACKNOWLEDGEMENT

The author wishes to acknowledge the advice and the assistanee of Dr. G. H. Beaton, head of the Department of Nutrition, School of Hygiene.

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Abstract –

Incidence of Laryngeal Involvement in Rheumatoid Arthritis; N.E.J.M.; 26 July, 62; Vol. 267, no. 4.

Of 100 patients with rheumatoid arthritis, 26% had laryngeal involvement. Their symptoms included:

1. Sensation of foreign body in throat.
2. hoarseness
3. fullness and tension in the throat.
4. dyspnea.
5. radiation of pain to ears.
6. stridor at night.
7. dysphagia.
8. odynophagia.
9. pain with speech.

Arthritis of the crico arytenoid joint has two phases. The acute phase is characterized by redness, pain, and swelling. The chronic phase is characterized by joint ankylosis. *F.L.*

Obesity

J. B. Cullen 6T3

The overwhelming problem in North American nutrition is over-eating. Obesity is here dealt with in its many aspects.

". . . l'appareil regulateur du poids était simplement faussé sous l'influence de la suralimentation . . ."[1].

This was the conclusion of Babinski's brother in his classic "Gastronomie Pratique". The latter has been almost as great a contribution to the culinary art as the neurologist's plantar reflex was to medicine. Since that time the introduction of numerous new methods of investigation have failed to detect any significant defects in metabolism which can account for most cases of obesity, other than an excessive caloric intake. Obesity has, during the past few decades, come to be associated primarily with North America. It has been estimated that the people of this continent are carrying 125 million tons of extra fat[2]. Various surveys estimate that between 10 to 35 percent of the population are ten percent or more overweight[3]. Although I do not have comparable figures for other areas of the world, Western Europe is probably very close behind us. Obesity would appear to be a by-product of prosperity.

Is obesity a problem? Or should it be accepted as an inevitable, unimportant side-effect of our affluent society?

The misconception held by many that the corpulent members of our society are the most content and well adjusted, is far from true. Numerous psychological studies have repeatedly shown that the obese person, especially in the younger age group, is limited in physical, mental and social success. Fear of embarrassment and humiliation often force him to become withdrawn and secluded. In many cases this may progress to shyness, oversensitivity, easy discouragement and a tendency to depression. Weight reduction is often associated with a remarkable personality change. Almost invariably, the patient who has reduced his weight, claims that 'he has never felt better in his life', or that 'he feels like a new person'. Fortunately this a very potent stimulus to the overweight patient. Certainly the lack of attractiveness which obesity produces in members of the fairer sex should be sufficient stimulus for weight reduction.

Apart from the psychological and esthetic reasons for reduction, repeated surveys by insurance companies reveal that death rates in the obese are well above those for persons of normal weight, at every age and in both sexes. The over-all results state that rates increase by 150 percent in overweight men and 147 percent in overweight women[3]. People are not dying of obesity per se, but rather of its consequences. The most common causes of death are associated with degenerative diseases: hypertension, coronary heart disease and atherosclerosis. Other complications include diabetes mellitus, degenerative arthritis, gall bladder disease, toxemias of pregnancy and surgical and post-operative complications. In fact, the only common cause of death not affecting the obese person more commonly than the lean is suicide.

DIAGNOSIS OF OBESITY

In research projects, accurate measurements of body fat can be made using under water weights to calculate the percentage of body fat present. Special calipers have been designed to record the thickness of skin folds over designated sites on the body. It is very unlikely that the practicing physician need resort to these methods. In most cases of obesity the use of the well-known height-weight-sex tables will be adequate, provided one is aware of their inherent faults. Items not taken into consideration on most of these are the degree of musculature in men, and the size of breasts, buttocks and thighs in women.

When deciding on the desirable weight for any particular patient, note the above, plus, whether or not the person is of small, medium or large frame. The tables on the following page provide rough guides to the desirable weights[3].

ETIOLOGY

As stated earlier the cause of obesity is an excessive caloric intake. Numerous investigations have been conducted in attempts to implicate metabolic, hormonal and other causes. None have been successful, and all conclude that the cause of obesity is overeating. But of course, this does not solve the problem, as now we must decide what causes overeating.

Appetite Regulation

In spite of the fact that there are plentiful supplies

HEIGHT		WEIGHT		
		Small	Medium	Large
Feet	Inches	Frame	Frame	Frame
5	1	113	121	131
5	2	116	124	134
5	3	119	127	137
5	4	122	130	140
5	5	126	134	144
5	6	130	138	149
5	7	134	142	154
5	8	138	146	158
5	9	142	150	162
5	10	146	155	166
5	11	150	159	171
6	0	154	164	176
6	1	159	168	181
6	2	163	173	186
6	3	167	178	191

Table I. Men. Weight and height as ordinarily dressed without shoes or coat.

HEIGHT		WEIGHT		
		Small	Medium	Large
Feet	Inches	Frame	Frame	Frame
4	8	94	101	111
4	9	97	103	113
4	10	99	106	116
4	11	102	109	119
5	0	105	112	122
5	1	108	115	125
5	2	111	119	129
5	3	114	123	133
5	4	118	127	137
5	5	122	131	141
5	6	126	135	145
5	7	130	139	149
5	8	134	143	153
5	9	138	147	158
5	10	142	151	162

Table 2. Women. Weight in pounds as ordinarily dressed, but without shoes and heavy outer clothing such as suit jackets.

of food available in the Western world, not everyone becomes obese. There must be some mechanism which regulates appetite and caloric intake. It has been shown that lesions placed in the ventro-median nuclei of the hypothalamus produce a marked increase of appetite and hence of body weight. A lesion placed more laterally produces a complete lack of interest in food and resultant starvation. Jolliffe refers to this regulating centre as the *appestat*[3]. By stimulating a desire for food when there is a shortage of calories and suppressing the appetite when this is restored, the appestat provides a caloric balance and body weight is unchanged. The manner in which the appestat reacts to food intake is not clear. Nervous, chemical and thermal mechanisms are suggested.

Nervous stimuli may be produced by contractions of the empty stomach or by the presence of food in the stomach. The introduction of vagotomy to decrease gastric contractions has, however, not caused a significant associated reduction of hunger sensations.

Differences in the levels of glucose in arterial and venous blood may act as a glucose "potential", which when high, suppresses hunger. No evidence has been given to substantiate this theory.

The specific dynamic action of the metabolism of food produces a certain amount of heat which may act as a stimulus for the appestat. This is a rather poor explanation, since people who are warm with, for example, hyperthyroidism, diabetes mellitus and hyper insulinism are all usually hungry.

Genetic Factors

There is no doubt that some inherited factor is important in obesity. Surveys have shown that if both parents are overweight, there is a 70 percent chance of their children being obese. On the other hand, if neither parent is obese, there is only a 9 percent chance of the children being obese. Approximately 70 to 80 percent of obese people have a positive family history[3]. It is extremely difficult to decide what the genetic factor is. Jolliffe suggests that the appestat is set at a higher level, or that it is more susceptible to being re-set at higher levels later in life with the exposure to precipitants such as pregnancy. Of course it may be merely that the child learns bad eating habits in the presence of his corpulent parents and so reaches the same state. Studies with identical twins reveal that the weight varies more than any other factor, and that there is a much greater difference if they are reared apart.

Astwood defends the overweight members of our society by suggesting that obesity is an inherited disorder due to a genetically determined enzymatic defect. He postulates that the more serious complications and consequences of obesity are also due to the inherited enzymatic defect or defects. Being very sceptical about the claims that weight reduction actually reduces the incidence of these complications, he accuses physicians who subject their contented, corpulent patients to strict reducing diets, of inflicting outright cruelty[4]. One would suspect from this that Dr. Astwood may well be a member of the corpulent society himself.

Hormonal Factors

The idea that obesity is due to "glands" has long been an excuse presented by the public and by the medical profession. It is now known that any obesity occuring with most endocrine disorders is coincidental, and should be treated in the same manner as simple obesity.

Myxedematous patients and cretins are often considered to be obese. This is merely another of the many misconceptions about obesity. In a series of patients with primary myxedema, one third were found

to be below standard weight for their height, and only 60 percent either normal or above normal[5]. Any increase in weight has been shown to be due to the accumulation of myxedematous tissue plus an increased water retention. The latter being able to more than account for any increase by itself.

Disease of the pituitary can produce Cushing's disease and Fröhlich's syndrome-both considered to be associated with obesity. The former produces its apparent obesity by inducing a redistribution of fat from the limbs to the trunk, and causing spontaneous fractures of the vertebral bodies and hence the appearance of a shorter, heavier trunk. There is no evidence that actual obesity in Cushing's disease is due to anything than excessive intake. Fröhlich's syndrome is an extremely rare disorder of complete pituitary deficiency. It is characterized by very fat abdomens, breasts and upper arms and legs. Wrists and hands are very small. Sex organs and glands remain infantile. Mental retardation and somnolence complete the picture. In both of these rather uncommon diseases, reducing diets, without the use of hormones, produces weight loss.

In true cases of hyperinsulinism, hypoglycemia produces an increased hunger which can only be relieved by frequent eating. These people will often become obese, as their caloric intake will exceed their actual needs. However, measurements of blood sugar levels in the ordinary obese person show instead, elevated fasting and post-prandial levels.

Gonadal malfuntions are often linked with obesity. Before and after puberty, in both sexes, there are changes in the body distribution of fat. Before puberty, the lack of androgens in the male makes any excess fat appear in the sites characteristic for the female. The reverse occurs in the pre-pubertal female. This of course makes the appearance or any obesity more obvious, but from it we cannot conclude that the sex hormones or lack of them is the etiological agent. Post-pubertal eunuchs may be fat or thin; the post-menopausal weights of women show no abrupt rise. There is little evidence to support gonadal etiology.

Habitual Overeating

In some individuals a continuous, prolonged period of overeating tends to set the appestat at a new, higher level. Satiety is no longer able to be met with the normal food intake. As a result, bulimia will persist, and the patient himself is only aware of overeating when this new, higher level of satisfaction is surpassed. These are the patients who deny overeating. Social and psychologic factors play an important role as causes of overeating.

In areas of the world where the high quantity and quality of food are the constant topics of conversation in the home, there will be a tendency to over-indulge. Different cultures, races and religions place different emphasis on food, and hence on its intake. People in the 'cocktail-circuit' and on expense-account lunches will tend to yield to the calories. Alcohol is important, not merely for the caloric value it provides, but also for the narcotizing effect it has on the appestat producing an increased appetite. Wives who encourage husbands to 'clear up all the scraps' at the end of every meal, rather than using their igenuity in preparing other meals from them, encourages the very thing which they will later criticize. Chronic food tasters, especially cooks are obviously vulnerable.

Psychologic factors are very important in a few cases, but are rather uncommon causes of obesity. Some people with social, sexual or financial frustrations may turn to food as solace. These people may not wish to gain weight, but once a higher level is set for the appestat, it will remain regardless of whether the original stimulus remains or not. People with few or none of the normal interests in life may derive their only pleasures from eating. For these persons attempts at food restriction is both cruel and useless. There is another group of people who purposely overeat. These include the child whose nagging mother has prevented him from stopping when his appetite was appeased, and the ignorant person who thinks that he will derive added strength from his added intake.

In using psychotherapy with this group of people, it is important not to make the patient aware of the psychological aspect of his disease. In so doing many patients will be distracted from their all important reducing diet and never achieve the desired goal. Obesity in children is less often precipitated by psychologic factors, and the only psychotherapy required will be for the mother.

When considering psychological problems as etiologicfactors, it should be remembered that many persons with the same problems do not become obese, and that obesity itself may be the cause rather than the result of these conflicts.

Exercise Factors

Normally when physical activity, and with it caloric expenditure increase or decrease, food intake increases or decreases in proportion. However people with very low levels of physical activity do not usually reduce their caloric intake proportionately. This is evident in the increasing incidence of obesity in the middle-aged people who reduce their physical activity, but maintain their caloric intake. The inevitable result — obesity.

No Metabolic Defect

It has been suggested that some people have an inherent defect in their carbohydrate metabolism, involving a block at the stage of pyruvic acid-the latter being diverted to the synthesis of fat. Normal people merely increase their metabolism when eating carbohydrate, whereas those with the defect produce fat. This is a very convenient theory, but there are several objections. (1) There is no evidence that over-weight people cannot oxidize pyruvate. (2) The only known block of CHO metabolism at the pyruvate level is in beriberi; certainly rarely associated with obesity.(3) There is no truth in the idea that any one person can eat more or less food without changing weight.[6]

The same author shows that the claim that, some persons eating the same amounts as certain obese persons do not gain weight, is not a valid argument against the excessive intake theory. It merely illustrates that one person has a greater total energy expenditure at rest and at work. There is a great variance between individuals as regards the basal metabolic rate and the expenditure of energy for a given task. This in no way denies the idea that excessive intake produces obesity. "Excessive" is a relative term and varies from person to person. If 1000 calories per day are given to *any* person, in addition to his normal diet, he will put on weight.

TREATMENT OF OBESITY

Contraindications to Treatment

These are few in number and rarely if ever present a problem. The greater the degree of obesity, the fewer the contraindications. Disease such as hyperinsulinism and Addison's disease may become fatal with reducing diets. In the former, removal of the tumor will allow a reducing diet to be safely prescribed. With gout, a high protein diet will precipitate attacks. Peptic ulcers should be allowed to heal or at least become assymptomatic before treating any obesity. In cirrhosis, where most weight gain is due to water retention, reduction may be undesirable. Many neuroses may be aggravated by the removal of the 'release' provided by eating. Any persons with rapidly fatal disease, such as leukemia, should be allowed to eat what they wish. With tuberculosis and chronic ulcerative colitis, it is probably desirable to maintain a weight 10 percent above normal in order to better combat recurrences. There is no reason to withhold treatment from persons in the older age group, those who are 'naturally fat', pregnant women, or persons with heart disease.

Dietary Treatment

Only general principals will be discussed here. When dealing with a case, reference should be made to a standard textbook of nutrition in order to calculate the desirable weight, the required caloric intake, and the caloric values of various foods.

It is important to impress upon the patient the need for reduction and that it is a gradual process rarely accompanied by a rapid weight loss. A definite weight goal should be determined for each patient. This can be calculated from the daily caloric deficit. This figure multiplied by 0.002 will give the predicted weight loss per week in pounds.[3] The most commonly prescribed diets are 1000 to 1200 cal. per day for women and 1500 cal. per day for men.

Success can only be expected if the diet is made to suit the patient rather than attempting to force the patient to follow a specific 'textbook' diet. Inquiries about the patient's eating schedule, likes and dislikes, and financial status must be made. Note his race and religion; it would be rather sensless to prescribe a diet including foods which may be rejected on this basis. Instructions must be given in how to calculate the caloric value of foods. The patient should record everything he eats and its caloric value as estimated by him. This reveals how sincere the patient is in reducing his daily caloric intake, and whether or not he can accurately estimate the caloric value of various foods.

Exercise is always a useful adjunct to dietary therapy, provided that it is not so extreme as to increase the appetite. Walking is the best form of exercise to recommend. An additional mile every day will cause the loss of 10 to 12 lbs. in one year. Remind the business man who claims he exercises by playing golf that the three Tom Collins back at the club-house, or at the 10th. hole completely overcome his caloric losses on the course.

Drug Therapy

This form of therapy must be mentioned only to condemn it in the treatment of most obese persons. The same may be said of food fads such as the recently introduced liquid diets. The aim of the physician is to train the patient in the use of proper eating habits. The patient using drugs will not alter his eating habits, and he will not be made aware of the source of his problem-overeating. These drugs may find some use in patients in whom a rapid weight loss is desired, but should never be given on a long term basis. Most are appetite depressants and being sympathomimetic have many undesirable side-effects including addiction. Diuretics, bulk agents, sedatives, cathartics, and drugs

Continued on page 210

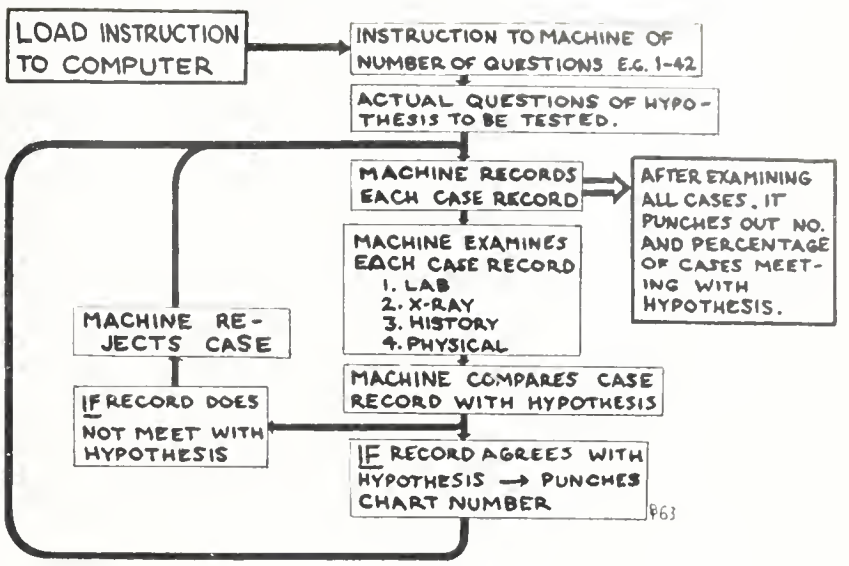
Recent Advances

THE DIGITAL COMPUTER IN MEDICINE

During the last decade there has been increasing awareness of the need for improved techniques in handling clinical and research data. The mass of data has presented difficulties in classification, correlation, search and storage. Recent advances in electronic data processing have indicated unlimited potential for the adaptation of such apparatus and techniques to the problem of clinical and investigative medicine. Initially, this type of apparatus was limited in its scope to statistical sorting and correlation studies of narrow focus because of the marked limitation of the quantity and type of data that could be handled. With the advent of the large scale electronic digital computer, its routine use as an adjunct to clinical and investigative procedures in diagnosis and therapeutics has become feasible.

There are two broad classes of electronic computers used for processing medical data: the *digital computers*, which use discrete electronic impulses in varying degrees to represent numerical or alphabetical information; and the *analogue computers* which use smoothly varying levels of electromotive force to provide an analogous representation of quantitative magnitude. The *analogue computer* is not suited for complex handling of large quantities of data. Its input is simple, its operations are manually controlled, and the results are obtained by means of meters or oscilloscopes. It is a comparatively small piece of equipment to be used routinely in the laboratory. The *digital computer* is far superior in its capacity to manipulate vast quantities of information in a complex manner, in multiplicity of types of input and output, and in its tremendous capacity for remembering. However, it requires several large pieces of equipment, special housing and special personnel for preparation of the data for processing and provision of instructions to the machine (programming). The digital computer consists of a magnetic memory drum which rotates at 12,500 r.p.m. It retains data stored on its surface in the form of magnetic spots and provides storage space for approximately 20,000 digits, each digit being identified by a pattern of magnetic spots. Large volumes of data may be stored in the drum in minutes or seconds from the card data or magnetic tape of the permanent medical record. The time required to locate any word varies between 0.096 and 2.4 milliseconds depending on the techniques of programming.

Evaluation of an hypothesis by a digital computer runs as follows (see figure). The machine is prepared by introducing instructions on the memory drum on how to perform the problem. These instructions (one set for each question in the hypothesis) are fed into the machine on cards. The hypothesis (e.g. this patient is acromegalic), and then the patients' records are fed into the machine. The machine scans each record in terms of the hypothesis. If the record does not agree with the hypothesis, the machine skips this record and passes on to the next case. If it does meet with the conditions of the hypothesis the machine records this case and passes on. At the end of the records the machine punches out a card with total number and percentage of patients whose records fulfil the hypothesis. An example of this will be given in the next issue.


LOAD INSTRUCTION TO COMPUTER
INSTRUCTION TO MACHINE OF NUMBER OF QUESTIONS E.G. 1-42
ACTUAL QUESTIONS OF HYPOTHESIS TO BE TESTED.
MACHINE RECORDS EACH CASE RECORD
AFTER EXAMINING ALL CASES, IT PUNCHES OUT NO. AND PERCENTAGE OF CASES MEETING WITH HYPOTHESIS.
MACHINE EXAMINES EACH CASE RECORD
1. LAB
2. X-RAY
3. HISTORY
4. PHYSICAL
MACHINE REJECTS CASE
MACHINE COMPARES CASE RECORD WITH HYPOTHESIS
IF RECORD DOES NOT MEET WITH HYPOTHESIS
IF RECORD AGREES WITH HYPOTHESIS → PUNCHES CHART NUMBER
P63

The question of 'machine-aided" medical diagnosis is a ticklish one. At the Rochester conference on data processing in July, 1962, the medical men in the audience claimed that it would be "a catastrophe to clinical teaching . . . resulting in the loss of the *art* of medicine". They pointed out the inability of the machine to distinguish between true symptoms and artifacts which a good clinician would easily spot. The engineers merely lowered their heads and smiled sardonically, for obviously the advance of "computerized" medicine has been relentless and progressive in spite of the protestations of the "true" clinicians.

H. Tanzer 6T4

This topic will be enlarged upon in the next issue of the Journal.

On Inspection

S. M. Zweig 6T3
D. P. Armitage 6T3

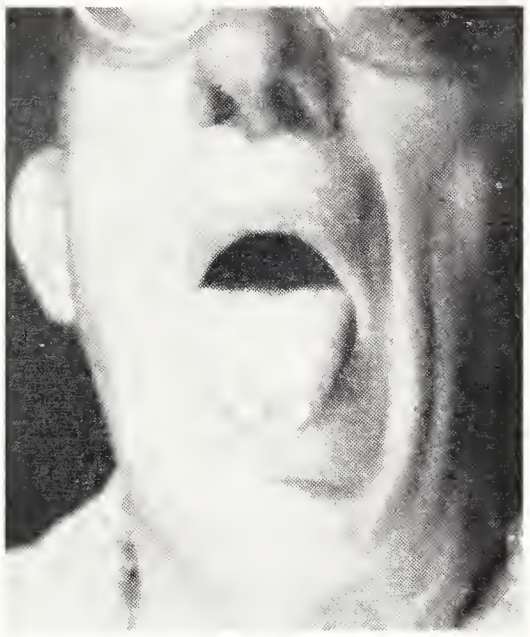


FIGURE 1: Note the smooth glossy tongue. In what conditions may such a picture present?

FIGURE 2: What broad diagnosis could be applied to this condition? What are some of the specific causes of this condition?

FIGURE 3: Note the elevated plaques; her blood sugar was 600 mg. %. What is the lesion called?

FIGURE 4: This patient's diet was remarkable in that it consisted almost entirely of corn, and lacked leafy green vegetables and animal proteins. The above pictured dermatitis developed during the summer (This patient's right hand is shown on the cover.) What is the likely diagnosis?

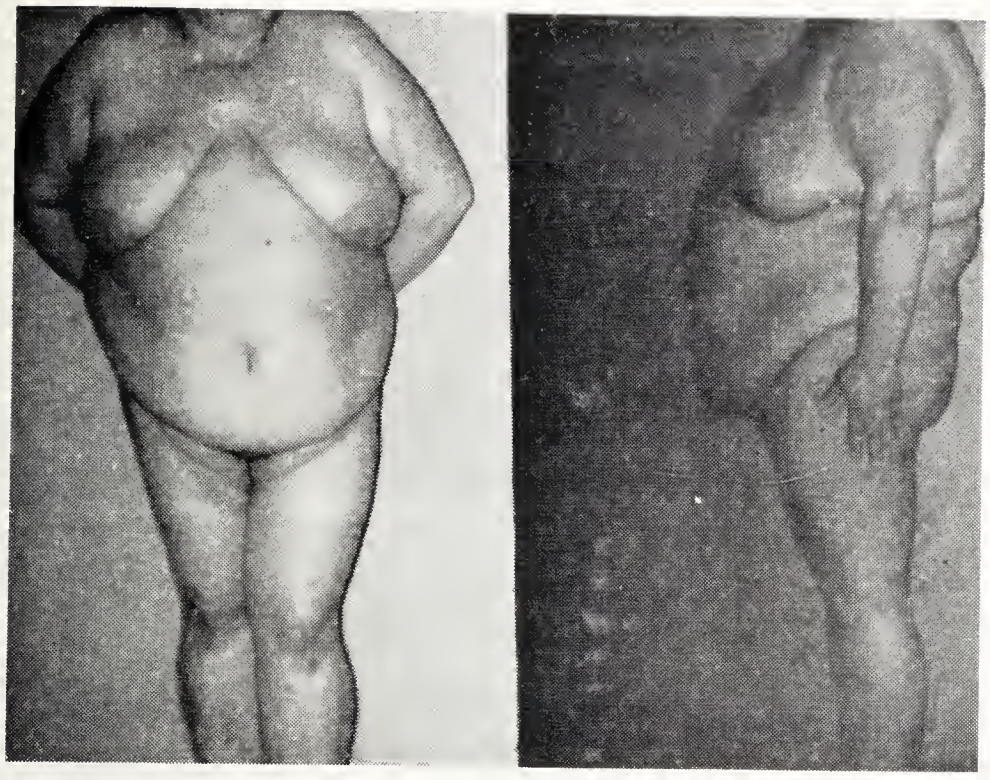
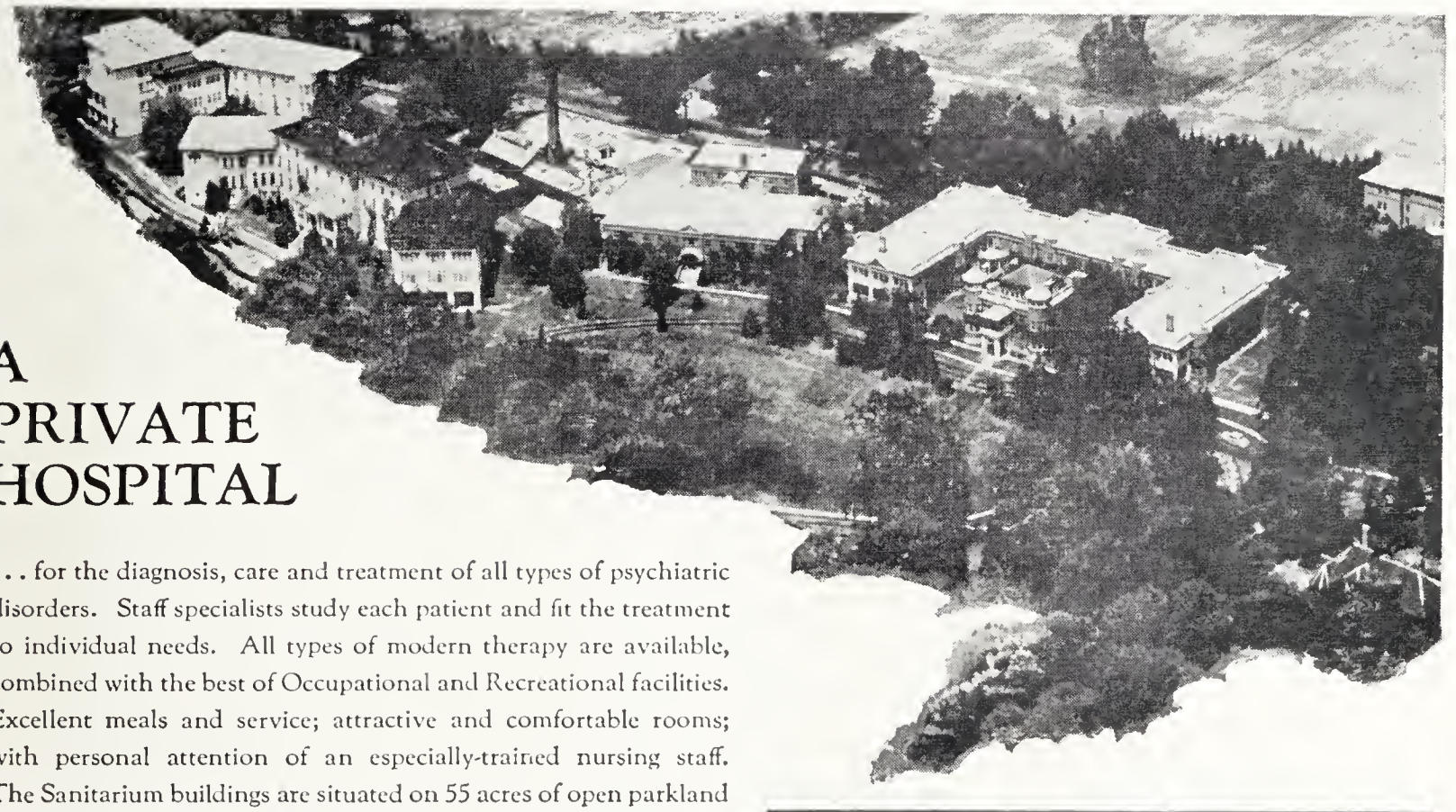


FIGURE 5: Weight: 310 lbs. Prognosis: death. Diagnosis?

FIGURE 6: Weight: 80 lbs. Prognosis: death. Diagnosis?

See page 212 for answers



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Malabsorption Syndrome

K. Moses, B.Sc. 6T3.
L. M. Geiger. 6T4.

A working classification of the malabsorption syndrome is provided in the following article, defining the primary and secondary types with appropriate methods of management.

The malabsorption syndrome may be defined as a symptom complex which results from impaired intestinal absorption of nutrients. The degree of malabsorption and the number of nutrients involved is variable. It may be limited to a single substance, or it may involve a broad spectrum of nutrients, such as carbohydrates, fats, proteins, amino acids, vitamins, minerals, water and electrolytes.

The first malabsorption syndrome was described in the Orient and was called *sprue*. The origin of the term, which means *thrush,* was from the thrush-like mouth lesions which were a prominent feature in this severe tropical disorder. Later, in Puerto Rico cases were noted to bear the stigma of this disease. A similar condition was found in non-tropical areas and was called *non-tropical* sprue.

The first documented description of the non-tropical condition in children, was made by Samuel Gee in 1888. He gave it the name *Celiac Affection.* The name was derived from the Greek word meaning belly, since the characteristic clinical feature was a distended abdomen, in an emaciated child. These children failed to gain weight and had large, pale, foul smelling stools.

During the German occupation of Holland in the last world war, when flour was not available, children with celiac disease were found to thrive. However, when wheat and rye flour were reintroduced into their diet, they suffered relapses. The reactive agent was found to be the gluten fraction of wheat and rye protein. This finding stimulated interest in the adult counterpart, non-tropical sprue. It had long been known that about half of these patients had had a history of childhood celiac disease. The removal of gluten from their diet resulted in improvement in a large number of cases. Thus celiac disease and non-tropical sprue were linked together.

Physiology

The assimilation of nutrients depends on two basic factors. *Digestion,* the preparation of nutrients by breakdown into smaller particles. *Absorption,* the process whereby these particles cross the intestinal mucosal barrier and enter the vascular system. The following brief discussion will point out a few of the highlights of these processes and to show how they may be operable in the development of malabsorption.

Digestion: *Digestive juices.* The various enzymes and other active substances in the juices are necessary for adequate preparation of the nutrients. Lack of bile occuring in conditions such as obstructive jaundice, limits the emulsification of fats, so that digestive enzymes have a smaller surface area on which to act. Pancreatic enzymes catalyse the breakdown of fats, proteins and carbohydrates; any condition leading to absence or deficiency of these substances result in malabsorption.

Time. Time is needed for adequate mixing of the ingested food with intestinal juices. If motility is increased or intestinal contents are diverted, the duration of mixing is decreased and absorption may be poor. Such a problem may arise after total gastrectomy.

Bacterial Flora. Normal intestinal flora aid digestion and may be the source of some important nutrients, such as vitamins K and B_{12}. Abnormal flora may compete with the body for the assimilation of foodstuffs, as seen in the blind loop syndrome, and post-gastrectomy.

Absorption: *Surface area.* The intestinal surface area is very extensive, because of the mucosal arrangement of crypts and villi. There are certain areas that are particularly important for absorption. Most nutrients are absorped in the first half of the bowel, whereas the terminal ileum is important for the absorption of fats, fat soluble vitamins and vitamin B_{12}. Extensive bowel resection or resection of the proximal jejunum of terminal ileum may result in malabsorption. Surface area may also be decreased if motility is increased and contact time with mucosa decreased.

Mucosal epithelial cells. These must be physiologically intact and functionally normal, since the absorption of many nutrients is dependant upon enzyme carrier systems in these cells. In diseases such as regional ileitis, the mucosal surface is damaged and its effective absorption is impaired.

Blockage of Lymphatic System. During digestion, fat is broken down into glycerol, fatty acids and monoglycerides. Fatty acids of more than ten carbon chains are routed as triglycerides into intestinal lacteals. Shorter chain fatty acids and glycerol enter the portal system. Blockage of the lymphatic system, for example by tumor, results in malabsorption of fat. Infiltration of the wall of the intestine as in Whipple's disease, amyloidosis, or lymphomas may cause malassimilation by a similar mechanism.

Classification

The malabsorption syndrome may be divided into two major groups, primary and secondary.

Primary Malabsorption

1. Celiac disease in childhood.
2. Adult non-tropical sprue. (Idiopathic steatorrhea.)
3. Tropical sprue.

Secondary Malabsorption.

1. Insufficient digestive juices.
   a. Bile.
      Obstructive jaundice, Severe liver damage (Cirrhosis).
   b. Pancreatic juice.
      Cystic fibrosis of pancreas (Mucoviscidosis), Chronic pancreatitis, Carcinoma of pancreas or ampulla, Inactivation of pancreatic enzymes (Zollinger — Ellison syndrome.)
2. Anatomical alteration in the G-I tract.
   a. Causing inadequate mixing.
      Gastrectomy.
   b. Decreased absorptive area.
      Resection of small bowel, Fistulae.
   c. Blind loop syndrome. (giving rise to abnormal bacterial flora.)
      Strictures, Surgical anastomosis, Diverticulae.
3. Diseases affecting intestinal mucosa.
   a. Tuberculosis.
   b. Crohn's disease. (Regional ileitis.)
   c. Scleroderma.
   d. Amyloid infiltration.
4. Miscellaneous.
   a. Protein loosing gastroenteropathy.
   b. Lymphatic obstruction — Lymphomas, Whipple's disease.
   c. Post therapy eg. Neomycin.
   d. Diabetes.
   e. Parasitic infestation.

Clinical Manifestations

Because of the numerous etioloical factors, the clinical manifestations of malabsorption syndrome in the broad sense are extremely variable. The characteristic pathophysiology giving rise to the clinical signs and symptoms are depicted diagramatically in figure 1.

From the diagram it is noted that the condition may present with one or more of the following; general malnutrition, diarrhea, hemorrhagic phenomena, osteomalacia and /or osteoporosis, edema, megaloblastic and/or iron deficiency anemia, glossitis and cheilosis, and peripheral neuritis.

In most cases of both primary and secondary sprue, the onset is slow and insidious. *Diarrhea* for months or years may be the presenting symptom but it is not unusual to elicit a history of relatively normal stool habits, except for unusually large volume. During exacerbations steatorrhea is always present, resulting in light-coloured, frothy, foul smelling stools, associated with explosive flatus. As the condition becomes more severe, the absorptive defect increases, and then simple water soluble compounds may be poorly absorbed. In fulminating sprue, malabsorption of nutrients may be almost complete, and even ingested water may be retained in the lumen with other ingested nutrients.

Fat is generally a large source of calories, and since fat is poorly absorbed, progressive *loss of weight* results. The amount of protein absorbed is also reduced. Thus endogenous proteins are used giving rise to muscle wasting, another prominent feature. Hypoproteinemia produces osteoporosis and pheripheral edema.

Another striking clinical feature, particularly in children, is the grossly *distended abdomen.* Not infrequently it has been observed that the distension progresses during the day, but disappears at night. It is due to abnormal motility of the G-I tract and an increase in the intraluminal content of fluid and gases. Vitamin D deficiency and hypokalemia are thought to be contributory factors.

Calcium deficiency may present in various ways. Its poor absorption is aggravated by combination with fatty acids in the intestinal lumen to form calcium soaps which pass through. Hypocalcemia may be manifested by spontaneous fractures of long bones due to osteomalacia, or by muscle cramps and tetany. However, parathyroid hyperactivity may compensate for this deficiency so that not all patients with low calcium levels will have symptoms of hypocalcemia.

The *hematalogic picture* in these patients may show hypoprothrombinemia, which if severe can cause a bleeding tendency. Inadequate absorption of the fat soluble Vitamin K is implicated. Macrocytic anemia, due to folic acid and Vitamin B_{12} deficit, may be complicated by the microcytic hypochromic anemia of iron deficiency. A double red blood cell population or dimorphic anemia can be present.

The diarrhea as well as poor absorption may cause excessive *loss of electrolytes,* especially potassium. Severe lassitude and fatigue may result. In severe cases, nausea and vomiting with abdominal pain may be noted.

Glossitis is seen at some time in all patients with chronic malabsorption. It may be limited to the tip of the tongue, or may be widespread giving rise to

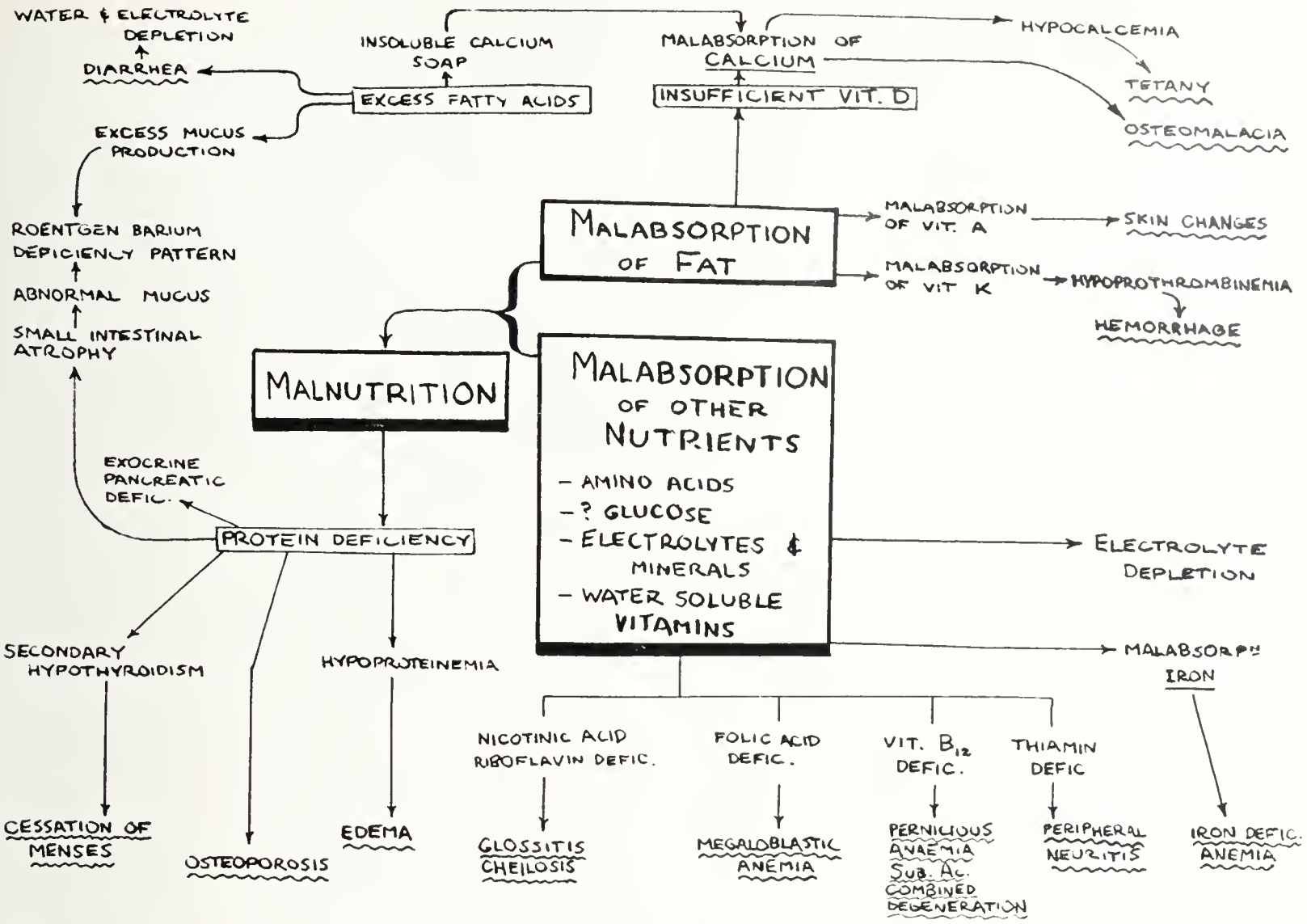

Figure 1. The pathophysiology of the malabsorbtion syndro ne. Possible presenting features are underlined.

denudation of the papillary surface with numerous aphthous lesions. The glossitis aggravates the malabsorption as dysphagia decreases food intake. In general, the appetite is good or even excessive in the presence of weight loss. During exacerbations however, anorexia is the rule.

Laboratory Diagnosis of Steatorrhea

Since steatorrhea is almost always present in malabsorption, the aim of laboratory investigation is to confirm the presence of excess fat in the stools and determine its cause.

The *gross appearance* of the stool may be normal; however, frequently frothy, greasy, pale, foul-smelling stools are present. Microscopic examination with a fat stain may reveal globules of fat, but this procedure is unreliable. Daily recording of *stool weight* may be helpful. A weight of over 400 grams suggests steatorrhea.

Stools may be collected for three days for the *estimation of fatty acid*. If more than 6 grams of fat is excreted, the diagnosis is probable provided the patient is on a constant diet containing 50 grams of fat or more. *Fat balance studies* are a more precise measure of steatorrhea. Faecal fat is determined over a three day period while the patient is on a measured 100 gram fat diet. Normally the fat excretion is 6 Gm./24 hr. or less. *Radioactive fat excretion* is a less accurate, but simpler method. 50 microcuries of I^{131} Triolein is given orally. The stool is collected for 72 hours and blood is drawn hourly for 5 hours. If the blood contains less than 10% of the ingested radioactivity, and the stool, more than 5%, the diagnosis of steatorrhoea is probable.

Investigation of Steatorrhea

Blood work. Blood may reveal a macrocytic anaemia, low plasma prothrombin and lowered serum proteins. The serum calcium may be lowered and alkaline phosphatase elevated as expected in hypocalcemia and osteomalacia. Serum sodium and potassium may be abnormally low. Fasting levels of particularly carotene and vitamin A may show deficiencies. A serum carotene level of 50mg/100 ml. and a vitamin A level of 60-100 micrograms/100 ml. is considered normal. Other substances such as cholesterol, iron and vitamin C may all be lowered.

Vitamin B_{12} Absorption (Schilling's Test). Radioactive B_{12} is given orally and urine collected over

the next 24 hours. The circulatory system is flooded with nonradioactive B_{12} one to two hours after the ingested B_{12}. Normally 11 to 26% of the radioactive B_{12} is recovered in the urine following the flooding dose. In pernicious anemia and in malabsorption, it is less than 8%. If intrinsic factor is added in pernicious anemia, the level returns to normal.

X-rays. Chest x-rays may show evidence of tuberculosis or mucoviscidosis. A flat plate of the abdomen may detect calcification in the region of the pancreas. A *barium meal* may be helpful, but diagnosis cannot usually be made on this basis. The so called "deficiency pattern" may be seen in severe cases of ideopathic sprue, but is just as often seen in secondary sprue. X-rays show dilatation, segmentation and flocculation of barium. These findings are thought to be due to changes in motility and hypersecretion of mucous. In pancreatic malabsorption the findings are normal. Evidence of fistula, diverticula or blind loop may be demonstrated by barium meal roentgenography.

Tolerance Tests. The *glucose tolerance* test is not as reliable, but is sometimes used. Characteristically the curve is flat in primary malabsorption. If a diabetic curve is found, pancreatic insufficiency is likely. The *D-xylose excretion test* is more reliable than the glucose tolerance. 25 grams of xylose in water is ingested. The urine is collected over 5 hours and tested for pentose. Normal values are five to eight grams over the 5 hour period. Sprue patients excrete 3 grams or less.

Other tests. Jejunal biopsy is helpful in the diagnosis of adult type sprue, celiac disease, and Whipple's disease. Findings are normal in pancreatic steatorrhea. Other tests, such as Secretin test, Pancreozymine test and Sweat test, may be used to diagnose muscoviscidosis and pancreatic steatorrhea. Indeed, a whole gammut of tests is at the disposal of the physician, and his investigation must be guided by the clinical picture, and his own intuition. Certain combinatons are suggestive of specific disease entities.

PRIMARY MALABSORPTION

We turn now to a brief consideration of primary malabsorption. Greater interest has been evoked in recent years since control or cure of this condition is now possible.

Nontropical Sprue and Celiac Disease

Clinical Picture. This is typical of the malabsorption syndrome with fatty stools, disturbed calcium balance and severe anemia. The abdomen may be distended with gas and fluids. Weight loss in the adult and failure to thrive in the child may be the presenting symptom, with superimposed irritability and lassitude.

Pathology. At autopsy, the findings are disappointing. There may be varying degrees of atrophy and slight thinning of the intestinal wall. Instead of the usual velvety appearance, the mucosa may be smooth and grey. With jejunal biopsy, histologic studies are possible in the living patient. The microscopic specimen often shows blunted, widened villi and deep elongated crypts. The epithelial cells are immature and hyperplastic. There may be chronic inflammatory cells in the lamina propria. By histochemical means, the enzyme functions of these epithelial cells are shown to be altered. Mitochondrias of the cells are enlarged and vacuolated as compared with normal columnar cells of the small intestine. Changes in the autonomic ganglia plexuses in the wall of the intestine have also been noted. Pathology, therefore, reveals a greatly decreased absorptive surface and morphologically abnormal cells.

Etiology. Most child celiacs and over half of the adult celiacs on a gluten-free diet improve markedly, demonstrating the deleterious effect of gluten on their gastrointestinal system. Gluten is found in wheat and rye flour (also possibly oats and barley). It can be broken down into several fractions, the active agent being a low molecular weight, heat stable, ultrafiltrable substance which is resistant to peptic/tryptic digestion and destroyed by enzymes present in pig intestinal mucosa.

Two major defects are apparently present in the development of the disease: mucosal damage and defective motility, which may be more important. Several theories have been postulated to account for the disease.

Allergic theory. Some observations in celiacs are suggestive of and compatable with an antigen/antibody reaction. The singleness of the deleterious agent, the response to corticosteroid thereapy, and the fact that even a taste of gluten evokes exacerbation may indicate an allergic basis. Even if allergy is not the basic mechanism, there is a greater tendency for celiac patients to develop secondary allergies, possibly because of incomplete protein breakdown and the damaged mucosal wall.

Toxic hypothesis. Gluten reintroduction into the celiac's diet causes hypo-motility and dilation. In vitro experiments have shown decreased peristalsis of isolated rat intestine when digested gluten is applied to the outer wall of the intestine. If the substance is applied to the normal mucosal surface, there is no such effect. The inhibitory action has been shown to be directed against the production of acetyl choline. The normal small bowel mucosa may contain enzymes which render the deleterious agent present in wheat gluten innocuous. In celiacs, therefore, an obvious assumption is an inadequacy of an enzyme system in

the mucosal membrane necessary for detoxification. Supporting evidence is the possibility that celiac disease is more prevalent in the relatives of these patients than in the general population. However, direct is lacking.

Tropical Sprue

Although essentially a disease of warm climates, tropical sprue may develop for the first time in temperate countries in individuals who have previously resided in the tropics or subtropics. It generally occurs after middle age, and very rarely affects children.

The etiology of this condition is still in the stage of postulation. Nutritional deficiency, jejuno-ileal insufficiency, bacterial or viral agents have all been implicated. However dramatic response to antibiotic therapy, seems suggestive of an infectious origin, although, as yet, no organism has been incriminated. A frequent suggestion is that rancid fats might constitute a local dietary factor of importance in the etiology of tropical sprue.

The patho-histologic picture is very similar to that of non-tropical sprue and celiac disease, so that it would be impossible to distinguish between them by this means. Along with dramatic clinical improvement, biopsy following administration of folic acid to such patients, shows regeneration of villi.

Clinically, there is a tendency for a more dramatic appearance in tropical sprue, and a shorter history. Frequently glossitis and diarrhea are the presenting symptoms. Anemia is more pronounced, even in the early stages. Hepatomegaly and plenomegaly are accompanying features.

Treatment-General

Regardless of etiology, certain general therapeutic principles are applicable to all gross steatorrhoeas.
General support and rehabilitation of body nutrition is essential. Parenteral measures may be necessary in severe cases.

Increased dietary fat; although increasing the steatorrhea, allows more fat to be absorbed, and therefore provides more calories. Approximately 70 Gm of fat is generally chosen. If diarrhea is present, fat restriction to 40 Gm or less is advisable.

Water soluble *vitamin K* (Mephyton) prevents hypoprothrombinemia.

Calcium and vitamin D therapy gives rise to a positive calcium balance and protects against ostemalacia. Large amounts of skim milk is one source of adequate calcium. Calcium supplements (calcium lactate) in amounts of 5 to 10 Gm daily may be prescribed. Vitamin D given orally 25,000 to 60,000 units daily in the oily form over prolonged period is sometimes required. The amount of vitamin D must be adapted according to need, as overdose is by no means desirable.

Vitamin B_{12} in weekly injections of 100 micrograms. may be necessary early in therapy. However these vitamins should not be used except when deficiencies are evident.

When *iron* deficiency anemia is present, oral *therapy* may be tried, but may not be absorbed, and replenishment of iron by injectable preparations is indicated. These patients must be watched and therapy dropped when the hemoglobin reaches normal limits. This caution avoids hemosiderosis.

Sodium, potassium and water depletion results with severe watery diarrhea. These patients must be rehydrated and their electrolytes corrected.

Specific Therapy

Nontropical sprue and celiac disease. The two most important therapeutic agents in each of these conditions are a gluten-free diet and adrenal steroids (or ACTH). A remarkable response may result from either therapy, steroids being used for the acute stages, and gluten-free diet, as the standard long term therapy. When a gluten-free diet is prescribed, it must be rigidly followed. It is important that the patient be vigilant about unexpected foods which might contain wheat. Response to diet is slower in adults than in children, in whom it is evident in three to six weeks. A trial of at least three months must be given in the adult before excluding gluten as the cause of their malabsorption.

In acute or resistant chronic sprue or celiac conditions, the administration of steroid drugs may yield excellent improvement, with marked increase in absorption in 24 hours. It therefore may be life-saving in acute fulminating cases. The mechanism of action is unknown, however all nutrients are better absorbed. Prednisolone, 15 to 20 mg. daily is the usual dosage. Relapses occur two to three weeks after discontinuing the drug. Antibiotics are of no avail in these conditions.

Tropical Sprue. Unlike nontropical sprue, tropical sprue responds well to treatment and complete cure is the rule. A gluten-free diet is of no value but patients are placed on a high protein, low fat diet. Folic acid and folinic acid seem to constitute specific treatment. Sometimes the response is inadequate and oral chemotherapy is then indicated. Short courses of antibiotics, two or more drugs given simultaneously are usually effective as a complete treatment. Some of the recommended drugs are succinyl-sulphathiazole, chloromycetin and chlorotetracycline.

Profiles

Dr. R. M. Price

A change will take place in the Faculty of Medicine this summer, and it is one that we shall all regret has occurred. In June, Dr. Price is retiring from active teaching in the Department of Bacteriology after twenty eight years on staff.

Dr. Price made her home in Vancouver and there she studied at the University of British Columbia. She subsequently took her degree in medicine at Toronto and interned in pediatrics at the Columbia Universty Division of Bellevue Hospital. Following this, she returned to Canada, and took up the problem of bovine tuberculosis in children with a grant from the National Research Council. It was largely the result of her work, that pasteurization of milk became law in Ontario in 1934.

Dr. Price began to teach in bacteriology in that same year. Her interest had always been tuberculosis, but in particular its manifestations in children. She has worked on BCG vaccine and was the first to introduce it here. It is no small measure of the regard that students have for her, that there was 100% acceptance of this new and controversial vaccine by her classes at that time. Her post graduate studies in these fields took her abroad several times, to the universities of London, Cambridge, Oxford, Copenhagen and others. In recognition of her work she was awarded the Starr Gold Medal by the University of Toronto.

Since the time that she started to study overseas, when she had some time left for visits to the continent, Dr. Price has been fond of travelling. This has not been confined to Europe, and she has taken many trips to the West Indies and South America. The one area remaining which especially attracts her is the Orient, in particular China and Japan. Esthetically, she is an earnest admirer of beauty in any form, but more so in music. Here it is the ballet, the great symphonies and the piano concertos which she enjoys the most. She also has a deep fondness for flowers and for many years has wanted to have a garden — a difficult thing in Toronto. Perhaps she will have more opportunity now.

Certainly we shall be sad when Dr. Price leaves this university. She is known and remembered by hundreds of students, and there is a feeling of great respect and admiration for this lady, who cared so much that we should be good practitioners of medicine and who spared no effort to help us in this respect. We wish her good fortune wherever she goes.

Jarda Polak 6T4

Continued from page 197

Other. In the blind loop syndrome; corrective surgery where possible is preferred; otherwise antibiotic therapy is instigated. In pancreatic and hepatic insufficiency; pancreatic and bile salts should be supplemented. In general, when the etiology is known, specific therapy is indicated.

ACKNOWLEDGEMENT

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Hospital Dietary Services

*Elizabeth B. Chivers BSc. HEc. RPDt.**

The author presents briefly the function of a hospital dietary department, its efficient use, and suggestions for improvement.

The aim of any food service is to serve the most nutritious food at the most reasonable cost. The dietary department as you are aware is an important phase in the hospital organization. It is responsible for approximately 10% of the total hospital budget.

A well organized dietary service is known to be one of best public relations agents to be found. There are several ways a favourable reputation is established with the public. Good food is served to patients and personnel. Through contact with the patients we let them know we are interested in their welfare. A good service will provide a restaurant where their friends may have a meal.

Departmental responsibilities in a hospital include maintaining and improving the nutritional status of patients and personal through meals planned, prepared and served according to the latest information available in foods, nutrition and institution management. The teaching of patients on special diets must be undertaken so that the prescribed routine can be carried out in their homes. The amount of money necessary, the time and equipment available for food preparation must all be considered in assessing their home situation. The department also provides specifieations for food, equipment and supplies; keeping equipment in running order; establishes and maintains sanitary standards in production and service areas; and hires and trains employees.

Every department in a hospital is to some degree "a world unto itself," yet each one depends upon the co-operation of the others for its sucecssful operation. The dietary department however is somewhat unique in that its function is more personal and affects more people in the hospital than all others. Patient or employee, every person who eats within the hospital evaluates the food to his own standards, considers himself an expert, and knows what he likes. There is a close relationship between food and morale. Thus it can readily be seen with or without just cause the dietary department is always exposed to criticism. The day has passed when the mere preparation of food-stuffs is all that is necessary. Diet is now recognized as a therapeutie tool essential in the management of any patient.

In a hospital, complaints about food are common, in many cases the quality may justify the dissatisfaetion but there are other factors which I would like to point out. Illness of any sort generally reflects itself in loss or change of appetite. A patient often looks forward to his meal as a break in hospital routine and thus may be disappointed when it arrives. Also preparing food in quantity is not easy, especially if one seeks a common denominator in taste. The mere fact that the patient knows he has no alternative but to accept the hospital meals can also serve as a source of irritation. The feeling of insecurity and resentment whieh a patient may experienee by relinquishing control of his aetions to hospital proeedures may reflect itself, not against some area of medieal care (of whieh he has little knowledge) but rather against something of which he is familiar — his food.

The dietary department, the kitchens, contain personnel who must give conseientious performance of duties and meet a deadline six times a day. Three meals and three nourishments on a limited budget. To do this and satisfy a multiplicity of tastes is not an easy task. The Canadian Council on Accreditation establishes certain standards which must be met in this area. For instance all local sanitary eodes must be met in storage, preparation and distribution of foods. In addition the department must be under the supervision of a qualified dietitian who is a member of the hospital staff. To be a successful unit, the fullest cooperation must be offered at all times.

From the medical and surgical staff we look for diet prescriptions that are realistic and aeeessible for patients being discharged. Protein, fat and carbohydrate content as well as calories should be detailed for diabetic patients. Fluid and ealoric content should be detailed for duodenal feedings. It is helpful if gastric diets, not from the diet manual of the hospital, are detailed. Low sodium diets must be specifie as to the amount of sodium restriction.

**Miss Chivers is a graduate of the University of Manitoba and the Vancouver General Hospital and at present is head of the dietary department at Queensway General Hospital, Toronto, Ontario.*

We of the dietary department are an integral part of the hospital team. One of our functions is to apply our specialized knowledge for the interpretation and facilitation of therapeutic diets. We do not presume to prescribe as that would be usurping the doctors role. We do place ourselves as a consultation service though, to help the doctor through advice and interpretation.

To provide a better service from a dietitians point of view, I would like to see several proposals considered. These include more clinical discussions and lectures for medical students with emphasis on basic nutrition and diet therapy, interdepartmental and interprofessional discussions of problems and policies, and ward rounds with the dietitian accompanying the doctors and nurses, especially with special diet patients. A diet manual would serve as a guide and aid in the clarification of dietetic terminology. With regard to individual diets, notification of changes of standard diets at least one hour previous to meal service, and diabetic diet changes implemented at the same time as changes of insulin dosage would improve the service. Requests for therapeutic diets should appear on the doctors order sheet and be signed by the doctor. Dietary orders for new patients, if available before the patient arrives, would allow meals to be served when the food is available.

In conclusion I would like to emphasize the fact that the dietitian is well trained and qualified to assume her place of importance on the hospital team. She is a professional woman engaged in an administrative capacity in a practical field with a broad educational background, a sound knowledge of nutrition and appreciation of the esthetic value of food. She also has a thorough appreciation of business practices, personnel management principles and the required skills. Members of the Canadian Dietetic Association are in every province of Canada. They must be fully qualified dietitians with a bachelor's degree from a university or college whose course contents meet the requirements of the Association. In addition they must serve an internship or have three years of diversified experience.

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Serum Protein Electrophoresis

D. P. Armitage 6T3

This article outlines the laboratory procedures used in examining serum proteins, giving suggestions regarding their clinical value at present and possible uses in the future.

The use of protein electrophoresis as a research tool is well established. In the biochemistry laboratory in many hospitals the separation of the serum proteins by means of paper electrophoresis is now becoming a routine procedure. When applied to the study of serum, urine and other body fluids in disease, electrophoretic protein patterns may be a practical diagnostic aid. Such is the case in kidney disease, multiple myeloma, agammaglobulinemia and macroglobulinemia. In many other disease states the electrophoretic protein changes are significant but not specific enough to be of diagnostic value.

The introduction of new supporting media such as cellulose acetate, and starch gel and the development of immunoelectrophoresis has greatly extended the application of protein electrophoresis in clinical research. The diverse nature of the work being done is exemplified by the following topics:

Blood proteins and electrolytes in allergic patients.

Plasma protein abnormalities in cancer.

Studies on the serum electrophoretic patterns in cardiac diseases.

Disturbance of plasma proteins in insulin shock in schizophrenic patients without metabolic disorders.

Many specific disease states have been investigated with regard to serum protein alterations for an interesting challenge exists in as much as diseases affecting every organ system of the body may have as a prominent biochemical abnormality an alteration of a serum protein which can then be evaluated.[1]

A brief outline of the various means of measuring serum proteins is presented with electrophoresis being covered in some detail. The major serum proteins, their known functions and the general factors influencing their concentration in the blood stream are discussed. The practical clinical application of serum protein electrophoresis is considered and evaluated.

Separation of Serum Proteins

The plasma of human blood contains an extremely complex mixture of simple proteins, lipoproteins, glycoproteins and other conjugated proteins. These proteins, with molecular weights ranging from 45,000 to 1,300,000, may exist in loose chemical combinations with such non-protein molecules as bilirubin, uric acid, calcium and injected dyes. The separation of this large heterogenous group of compounds began in 1852 when the plasma proteins were separated into two large classes, namely albumins and globulins, by precipitation of the globulins with a solution one-half saturated with ammonium sulfate. Various concentrations of different salts have since been used in salting out procedures and each solution has been found to produce precipitates composed of different heterogenous groups of serum proteins. Albumin and globulin concentrations have been examined for many years according to Howe's method (1921) whereby the globulins are precipitated by adding serum to a solution containing 22.2 percent sodium sulfate. Another fractionation procedure utilizing ethanol precipitation at low temperatures (Cohn)[2] and resulting in five components has been used but does not lend itself readily to clinical use.

Moving boundary electrophoresis devised by Tiselius in 1937 provided a great impetus to the study of serum proteins, and paper electrophoresis (a modification of Tiselius' boundary electrophoresis) has largely replaced salt fractionation as the procedure of choice for quantitation of the various serum proteins.

The separation of proteins by electrophoresis is based on the principle that proteins vary in their isoelectric points and will bear net charges of different magnitudes at any given pH. The individual components of a mixture of proteins will therefore migrate at different velocities when solutions of the protein mixture are subjected to an electric field. Molecular weight is also a factor in the rate of migration since the smaller molecules such as albumin migrate faster than the large molecular weight globulins.

The process of ultracentrifugation is used to assess the purity of various protein fractions and to estimate the molecular size of specific proteins. The lipoproteins have been studied by this procedure which has also facilitated the detection and separation of abnormal proteins.

The modern antigen-antibody theory of disease

states may well be established or disproved by immunoelectrophoresis for now, by means of this procedure, antibodies present in infections and allergic diseases can be isolated and identified. Specific single proteins have been studied and abnormal proteins have been separated by this method.

Separation by Paper Electrophoresis

At the Toronto Western Hospital the following procedure is employed. Approximately 5 cc. of blood is sent to the laboratory with each request for a protein electrophoresis. The procedure is divided into five phases:

Estimation of Total Protein. The total protein concentration in the serum is determined by means of a method based on the biuret reaction of proteins. This procedure requires 0.5 cc. of serum.

Electrophoresis. Strips of filter paper moistened with a barbiturate buffer (pH 8.6) are placed in Spinco Model R paper-electrophoresis cells and by means of special pipettes, 4 to 10 microliters (0.004 to 0.010 cc.) of serum, depending on the total protein concentration, is applied to the strip. The current is then turned on and migration allowed to occur for the next 16 hours at a current of 2.5 milliamps per cell. It is preferrable to carry out electrophoresis in a controlled environment and it has been found that a better separation of the protein fractions occurs when this procedure is undertaken in a cold room kept at 4 degrees Centigrade.

Staining. The strips are removed from the cells, rinsed in water three times, and then dried at 120-130 degrees Centigrade for 30 minutes to coagulate the protein. They are then pre-rinsed with methanol for 6 minutes in order to remove the buffer salts from the paper and then placed in a 0.1 percent bromphenol blue dye solution for 30 minutes. The strips are then rinsed in acetic acid to remove excess dye, partially dried between sheets of blotting paper and then further dried in an oven at 120-130 degrees Centigrade. The individual protein fractions (albumin, alpha$_1$, alpha$_2$, beta$_1$, beta$_2$, and gamma globulins) which have bound the dye appear as blue-green bands of varying intensity depending on the concentration of protein present. Immediately prior to scanning, the electrophoretic strips are exposed to ammonia vapours to bring about intensification of the dye and the density of the band is measured photometrically by means of a densitometer.

Quantitation is accomplished with a Spinco Model RB analytrol which performs the functions of a densitometer and an intergrator. The densitometer measures and records the amount of light absorbed by material distributed along a paper strip which is passed in front of the measuring photo cell. Variations in the amount of light absorption are recorded by a recording pen as a curve on the graph. Operating simultaneously with the densitometer the integrator automatically quantitates the area under the curve and records it on the same graph as a sawtooth pattern. Each 0.1 sq. cm. of the graph found under a given peak is represented by a single sawtooth deflection. The heavier integrator markings indicate an involvement of 1.0 sq. cm. of the graph surface. (fig. 1.)

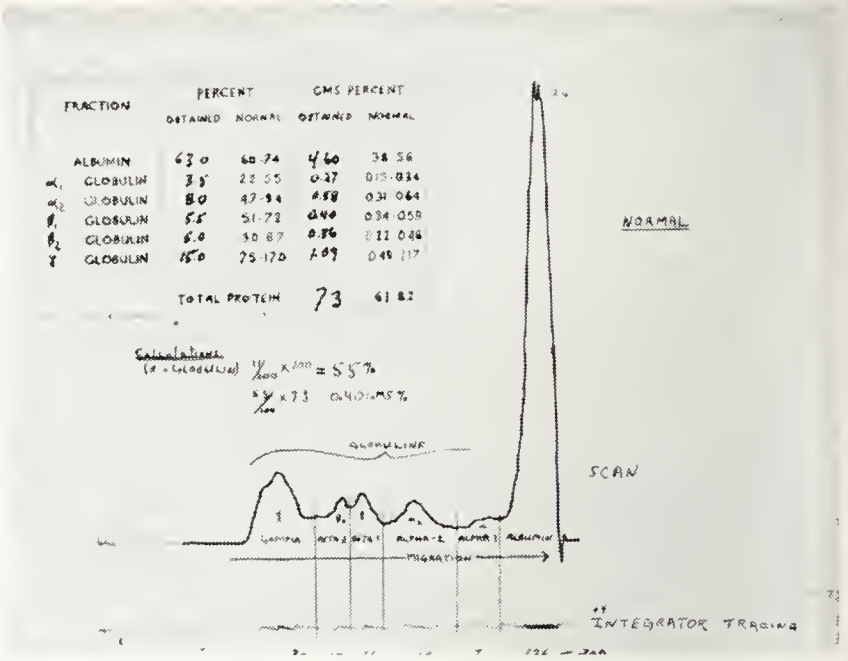

Figure 1. Normal Electrophoresis

Calculation. After the individual peaks have been marked off, the total area under the curve as well as the area under each peak is determined from the integrator tracing. The percentage of the total represented by each peak is then calculated and recorded in the left hand column. (fig. 1.) The absolute concentration in grams percent of each fraction is found by employing the known facts of total protein concentration and percentage values.

Duplicate electrophoretic separations are carried out on each serum sample and the results are accepted and reported if the percent of albumin on each scan agrees to within 3 percent.

Major Serum Proteins

Albumin, synthesized in the liver, is a simple protein with a molecular weight of 65,000. It is the smallest, most soluble and most electrically mobile of all the major serum protein components. The physiological functions of albumin range from a stabilizer of blood volume regulating the distribution of water between the intravascular and interstitial compartments of the body, to a transport protein for such compounds as

uric acid, bilirubin, certain drugs, and the following dyes: phenosulfonapthalein, bromsulfalein, Evan's Blue, Congo Red. It is thought to influence the excretion and diffusion into tissues of globulin-bound substances such as copper, iron and thyroxine. Theoretieally albumin exerts a stabilizing or solubilizing effeet on the more insoluble globulins, especially the beta and gamma-globulins. Thus, in the presenee of normal amounts of normal albumin there tends to be no reaction in the flocculation tests. (Ccphalin-Cholesterol Floeculation; Thymol Turbidity; Zinc Sulphate)

Hyperalbuminemia is often associated with dehydration which may mask a normal or markedly decreased concentration of this protein. Hypoalbuminemia is more common and may be caused by one or more of the following conditions:

- Failure of synthesis (acute fulminating liver disease)
- Excessive loss — renal lesions
- Increased degradation of serum proteins
  - Thyrotoxicosis
  - Post operative convalescence
  - Burns
  - Chronic infections
  - Trauma
- Inadequate protein intake, absorption or utilization
- Dilution of plasma volume

The *globulins* are found in three main groups when studied by routine paper electrophoresis: the alpha, beta, and gamma-globulins. More than fifteen globulins have been obtained by other technics such as starch-gel electrophoresis.

The *alpha-globulins* comprise a heterogeneous mixture of serum proteins with molecular weight of 200,000 to 300,000. They are separated electrophoretically into two fractions, $alpha_1$ and $alpha_2$ globulins. Ceruloplasmin (the copper carrying protein), a complex constituting the protein bound iodine (P.B.I.) and 20 percent of the lipoproteins migrate with the $alpha_2$ globulins. The glycoproteins and the mucoproteins are also found in the alpha globulin fraction.

The *beta-globulins* which are also separated into two fractions by paper electrophoresis, $beta_1$ and $beta_2$ globulins are a group of unstable heterogeneous proteins with molecular weights of 150,000 to 300,000. The beta globulins contain 80 percent of the lipoproteins including most of the free and esterified cholesterol, phospholipids and some triglycerides. Transferrin (siderophilin), the iron binding protein is said to represent approximately one-third of the beta globulin fraction.[3]

Although relatively little is known about the alpha and beta globulins, it is felt that hormones of the pituitary, parathyoid and pancreas are localized in this group as well as enzymes which may have leaked out of intact or damaged cells. Non-speeifie changes in the alpha and beta globulins have been shown to oeeur under different pahologieal eonditions. For example, the alpha-globulins are increased in conditions having extreme tissue damage; the beta-globulins are increased in conditions accompanied by hyperlipemia. These inelude nephrotic syndrome, diabetes mellitus, hypothyroidism, xanthematosis, alimentary lipemia, idiopathic liver lipemia, and diseases of the liver and biliary tract (obstruetive jaundiee, biliary cirrhosis, aeute hepatitis, portal cirrhosis).

The *gamma-globulins* which have molecular weights ranging from 150,000 to 1,000,000 are thought to originate in the plasma cells and/or the eells of the reticuloendothelial system including its hepatie ramifieations. Almost all of the circulating antibodies and agglutinins are eontained in this fraction.

In eomparison with the alpha and beta globulin fractions, many facts are known about the gamma-globulin fraction. An inereased concentration has been known to occur from a stimulation or proliferation of the retieuloendothelial cells, or from an increase in antibody production due to infeetions or other diseases involving an immunological response. A deerease in the gamma-globulin concentration has been known to occur in physiologieal hypogammaglobulinemia of the newborn[2] and also in eongenital hypogammaglobulinemia or agammaglobulinemia. In certain cases no known cause for the lowered gamma-globulin eoncentration has been found. In other instanees a deereased gamma-globulin level has been shown to be secondary to other pathologieal eonditions such as inadequate protein intake, or excess loss due to a renal lesion. Certain disease states involving the reticuloendothelial system such as multiple myeloma, leukemia and lymphomatosis as well as some of the treatment given for these diseases (total body radiation, nitrogen mustard therapy) may decrease the gamma-globulin eoncentration. Cushing's Syndrome or the administration of adrenocortieal hormones may also result in a lowering of the gamma-globulin concentration.

Diagnostic Value of Electrophoresis

Many investigators have reported "significant" changes in the electrophoretic patterns of the serum proteins following investigation of speeifie diseases. However in most cases these changes are non-specific. In other cases the electrophoretic pattern may lead directly to the diagnosis.

Multiple Myeloma. In 75 to 90 pereent of cases of multiple myeloma a typieal pattern has been noted

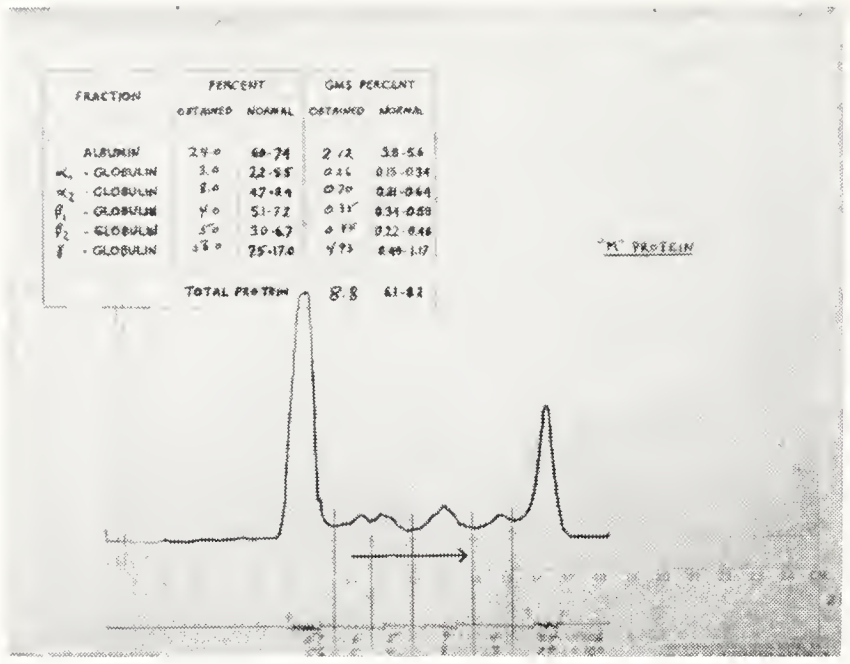

Figure 2. 'M' Protein.

with an abnormal sharp peak appearing on the electrophoretic tracing of the patients serum. This peak represents an abnormal, fairly homogeneous protein called the myeloma or "M" protein. Although the peak commonly appears in the gamma-globulin region (fig. 2) it may appear along with the alpha or beta globulins. The sharp peak of the myeloma protein contrasts with the diffuse hypergammaglobulinemia found in other disease states. Fodell has suggested a 4:1, height to width ratio, as being diagnostically significant for an abnormal myeloma spike protein[4].

Dunn[5] maintains that a serum protein peak in the alpha$_2$ globulin to gamma-globulin zone is almost pathognomonic for multiple myeloma. However, similar peaks occur in atypical macroglobulinemia and in macroglobulinemia of Waldenström (fig. 3). These three diseases must be differentiated by more refined techniques such as ultracentrifugation or immunoelectrophoresis (Korngold[6]). It has been found that the disease characterized by the appearance of macroglobulins in large quantities in the serum has a decidedly better prognosis than that of multiple myeloma where severe pains, bone destruction, anemia and cachexia usually develop quickly[7].

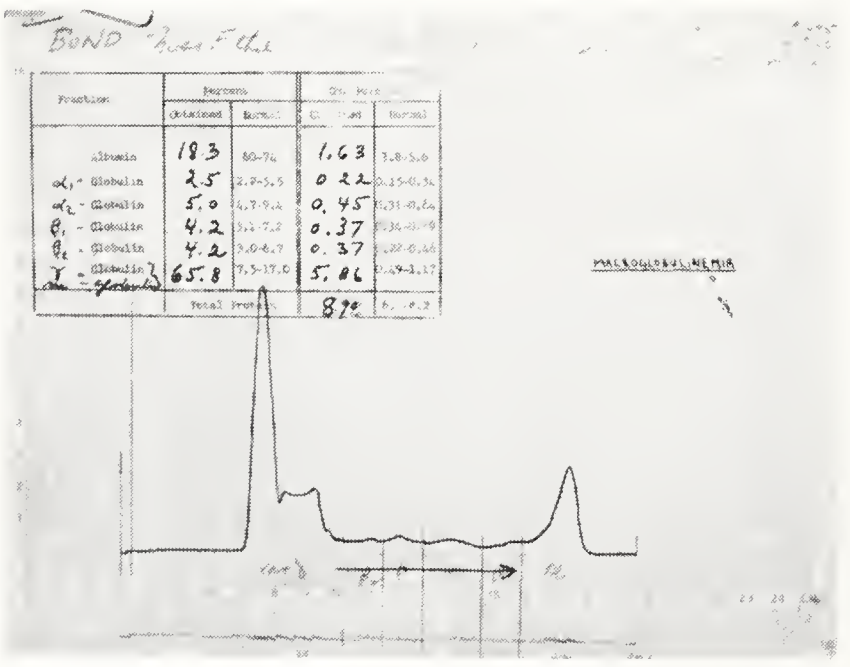

Figure 3. Macroglobulinemia

Essential cryoglobulinemia may also be confused with multiple myeloma. This disease state is due to a protein which has a non-specific electrophoretic behaviour simulating that of the gammaglobulins and a specific property of precipitating in cold. This latter property provides a means of distinguishing this protein from the myeloma protein.

Nephrotic Syndrome. In this disease state consistant findings in a high percentage of cases include a marked decrease in the albumin concentration and a moderate decrease in the gamma-globulins (fig. 4). A signficant increase in the alpha$_2$ globulins and/or beta-globulins may accompany the above changes.

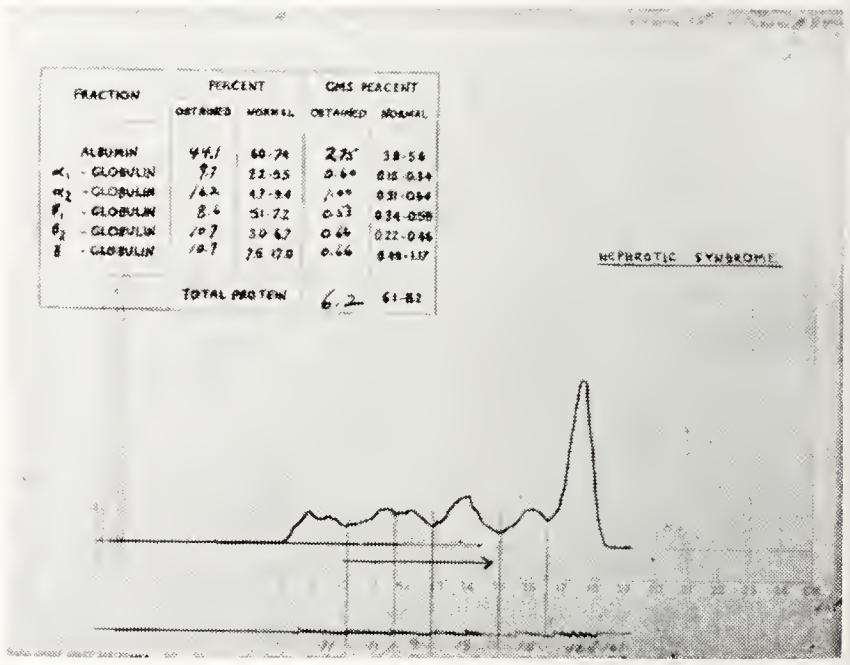

Figure 4. Nephrotic Syndrome

Hypogammaglobulinemia is diagnosed when the gamma-globulin level falls between 0.15 and approximately 0.5 grams percent. Below 0.15 grams percent a condition of *agammaglobulinemia* is said to occur.

Non-Specific Observations

The following findings, although not diagnostic have been observed by many investigators and are listed here to indicate some of the more promising fields of electrophoretic investigation.

1. There appears to be a direct relationship between the level of serum beta-globulins and atherosclerosis.

2. In general, normal serum proteins indicate good

health. This fact has been used to direct suspicion away from an organic illness as a possible cause of psychotic symptoms in patients with mental disorders.

3. Prognostic significance during the acute state of glomerulonephritis has been noted by Van Slyke[2]. Only 13 percent of cases maintaining a plasma albumin level above 2.2 grams/100 ml. progressed into the chronic or terminal stages of nephritis in contrast to 72 percent of the group with low albumin levels.

4. In one series of patients with serum globulins elevated to levels of 5 grams/100 ml. and higher, 90 percent had one of sarcoidosis, myelomatosis or a collagen disease[1].

5. A transient state of hypogammaglobulinemia has been found in 2 year old children with an unusual susceptibility to infections. This fact extends the differential diagnosis of sudden death in an infant and the post mortum investigations of such a case might well include serum protein electrophoresis[5].

Summary

The role of serum protein electrophoresis in the diagnosis of specific diseases has been studied. While claims have been made that certain groups of diseases such as malignancies or certain specific diseases such as cirrhosis produce characteristic abnormalties in the serum protein pattern the abnormalties observed prove to be common to a variety of disorders. In a few conditions such as the nephrotic syndrome and hypogamma or agammaglobulinemia, changes in the electrophoretic pattern are sufficiently specific to be of diagnostic value. Multiple myeloma produces a characteristic serum protein pattern but must be distinguished by means of other techniques from essential macroglobulinemia, macroglobulinemia of Waldenstrom and essential cryoglobulinenmia all of which can give similar patterns. Repeat protein electrophoretic determinations can be of considerable help in following the course of many diseases either during therapy or without treatment. Changes in the electrophoretic pattern towards normal are usually associated with improvement of the patient. A few of the diseases that might be followed electrophoretically are acute glomerulonephritis, severe or chronic illnesses, malnutrition and hypogammaglobulinemia.

Although Cohn's serum protein fractions are not used in clinical investigation they have been found to have valuable practical applications. Albumin (factor V) is used intravenously in cases of shock and in cases of hypoproteinemia. Factors II and III (the gammaglobulins) are used prophylactically against several viral diseases and in much larger doses as supportive therapy for patients with hypogammaglobulinemia or agammaglobulinemia. Factor I (fibrinogen and antihemophiliac globulin (AHG)) is used for certain problems of blood clotting.

Man's limited knowledge of the sites of origin, properties and functions of the serum proteins not only provides an immediate challenge but also allows some speculation as to the future of this relatively new laboratory procedure. The paucity of well established facts hampers an interpretation of the laboratory findings. Experience in reading the reports and a correlation of the clinical history have proved to be most helpful. To date the practical aspects of electrophoresis are somewhat limited, but in time, much valuable information may be discovered which will help not only in the elucidation of the pathophysiological changes in diseases but also in the diagnosis and treatment of an increased number of specific disease states.

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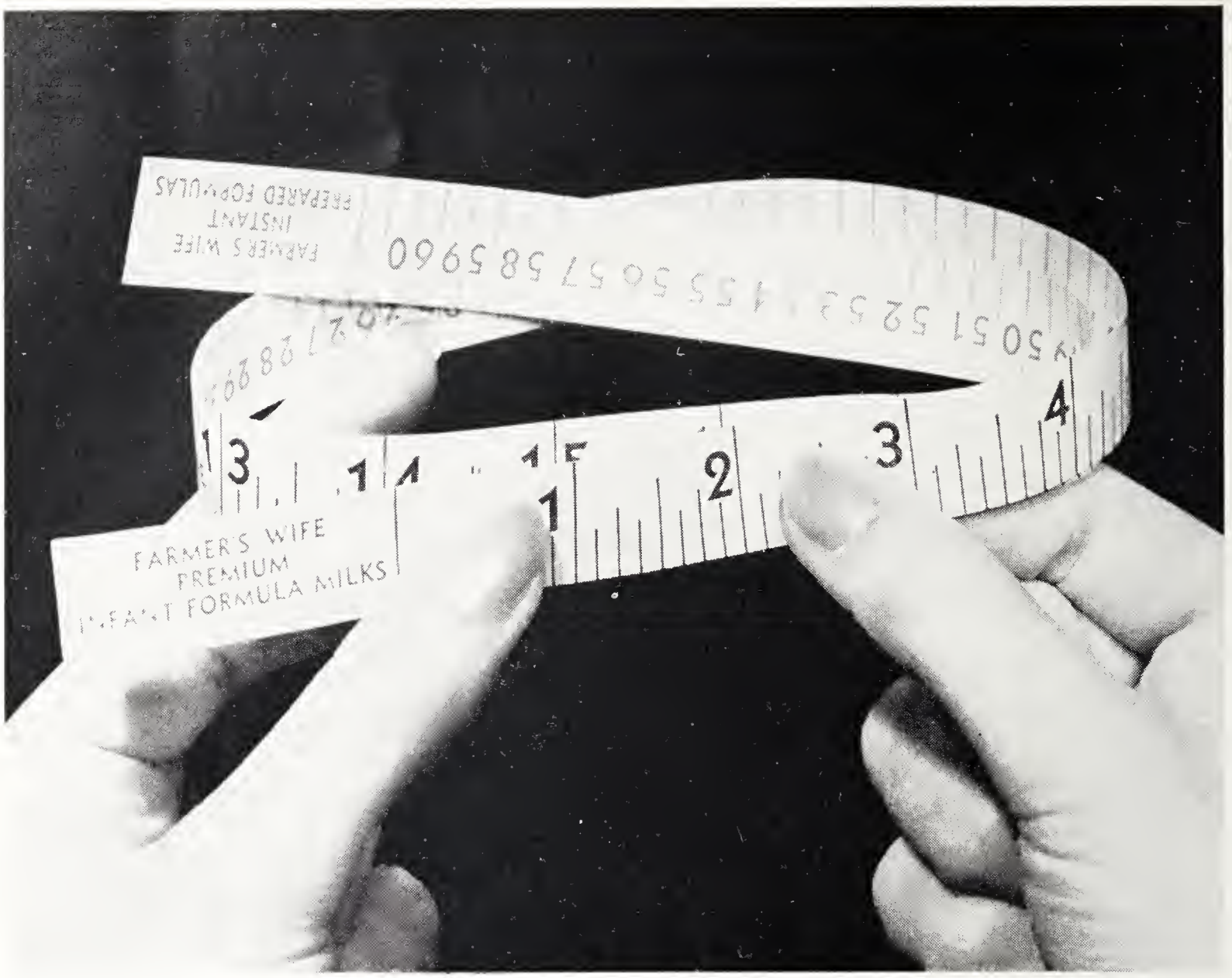

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The Immunological Function of the Thymus

Jerome S. Burke 6T5

As well as suggesting the thymus gland as a source of the small lymphocyte, the author raises the interesting possibility that it plays an important role in immunilogical phenomena.

The thymus gland, long known as an obscure collection of lymphoid or paralymphoid cells, has remained enigmatic until recently. During the past year, a flurry of reports have given the first indications of the role of this organ as possibly the "master gland" controlling the immune response. In mammals the thymus develops from the third and fourth pharyngeal pouches in early embryonic life, reaches maximal relative size near the time of birth, and then undergoes a gradual involution. In man, the thymus appears in the 10 mm. embryo, reaches maximal relative size in the neonate, attains maximal absolute size in the twelve year old child, and then gradually decreases in relative and absolute size as maturity is reached[1].

Each lobe of the thymus consists of numerous lobules held together by fibrous tissue. Individual lobules contain several follicles and each follicle has cortical and medullary portions. The cortex is composed predominately of lymphocytes, with some larger cells, thought to be lymphocyte precursors. The origin of these lymphocytes has long been in dispute. Some have held that they and their precursors migrate into the thymus from surrounding mesenchyme; others from entodermal cells of the thymus itself. Auerbach[2] has recently shown that the primitive entodermal cells of a twelve day mouse embryo thymus differentiate into lymphocytes upon transplantation into the anterior chamber of the eye in adult mice of the same strain, and will even grow and differentiate into lymphocytes under favourable conditions in vitro. Mesenchyme is necessary for this differentiation but acts as the source of an inducing agent rather than as the cell donor. Histologically, the thymus of the newborn presents the normal adult architecture and appears fully functional at a time when other lymphatic tissues are very incompletely developed.

Thymus and Immune Reactions

The importance of the thymus in immune reactions has been indicated by recent extirpation studies. Thymectomy of rabbits aged three weeks does not alter their capacity to make antibodies against protein antigens. However, Archer and Pierce[3] have shown that rabbits thymectomized at birth may have thereafter a diminished capacity to make antibodies. Rats, neonatally thymectomized, have a diminished capacity to make antibodies against and to develop Arthus sensitivity to bovine serum albumin[4]. The response of thymectomized animals was also impaired in a variety of delayed hypersensitivity reactions[5]. Miller[6] and Good[7] et al. have demonstrated that thymectomized newborn mice are unable to respond effectively to antigenic stimulation either in the form of homograft skin transplantation or of soluble antigens. Miller has also shown that replacement with intact viable thymus restores homograft reactive capacity in the mouse; injection of thymic homogenate does not restore immunological competence. Therefore these thymectomized animals are immunologically inert towards substances that would normally be expected to elicit an immune reaction.

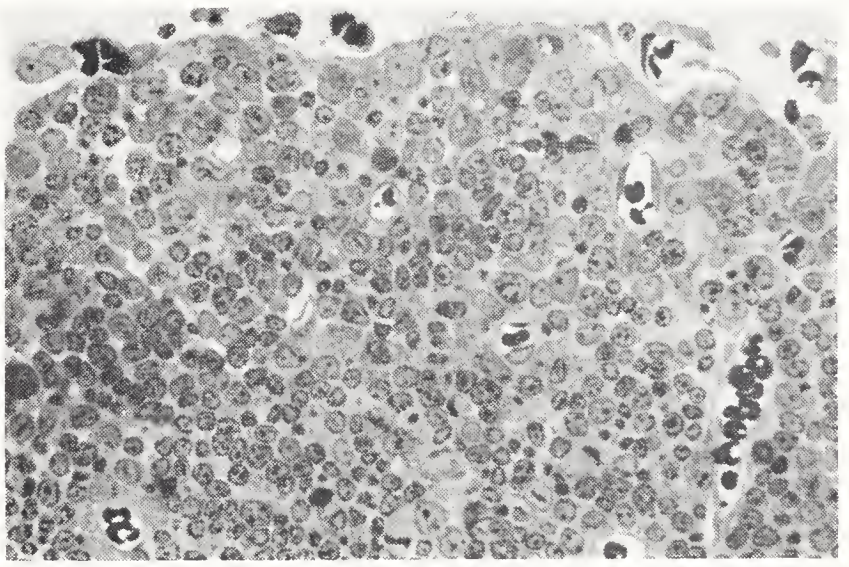

Figure 1. (X130X4.7) Thymic cortex of a 27 day old fetal rabbit showing the large light epithelial cells at the periphery, and the well developed small lymphocytes with dark chromatin granules in the centre. The few large cells with clumps of chromatin are probably lymphoblasts. (courtesy of Dr. H. Z. Movat)

These results can be correlated with the work of Mueller[8], who found that removal of the bursa of Fabricius in newly hatched chicks or prevention of the development of this organ by hormonal treatment interferes with the full development of immunological potential in these animals. The bursa, like the thymus in the mammal, is a lymphoid organ which originates as an endodermal-epithelial outpouching[9]; is of maximum relative size in the newly hatched animal and becomes spent and of lesser size as the animal approaches maturity. Both the thymus and the bursa appear to play key roles in the development of full immunological capacity in their respective hosts.

Perhaps the most striking fact established by these experiments is that thymectomy at any age from birth through childhood, is followed by a decrease in the peripheral blood small lymphocyte count[10]. The fall is slowly progressive over several weeks and the count is low for many months. In addition, the thymectomized animals show clear evidence of depletion of small lymphocytes in the spleen and lymph nodes. These organs are actually smaller in thymectomized animals. Microscopic examination of the spleen and lymph nodes in rats thymectomized at birth reveals an almost total absence of small lymphocytes; yet plasma cells are present in normal proportions and germinal centres are intact[11]. In contrast, Miller has reported a failure of germinal centre development in neonatally thymectomized mice[6].

Lymphocyte Depletion

There are two theories for the lymphocyte depletion in thymectomized mice. The *first theory* is that during natal and early post-natal life, the thymus is a major source organ of immunologically competent cells, which have to mature and then are distributed centrifugally to the spleen and other peripheral lymphoid tissues where they play an essential role in the immunological process. P^{32} studies measuring the relative rates of DNA synthesis in various lymphatic tissues of the rabbit have shown a greater rate of lymphocyte production at all ages in the thymus, compared to other lymphoid organs which appear to possess only a slight lymphopoietic function[10]. Sainte-Marie and Leblond[12] in a study of lymphocyte production in the rat thymus found a very high mitotic frequency in the thymic cortex. In the medulla, they noted cells of the lymphocyte series with irregular configurations suggestive of ameboid motion and observed diapedesis of small lymphocytes into the endothelial-lined, perivascular, presumably efferent lymphatic channels. They also suggested that the thymic medulla might contain a factor, possibly secreted by reticular cells, responsible for attracting lymphocytes from the cortex to the medulla and perhaps responsible for their diepedesis across the endothelial channels as well.

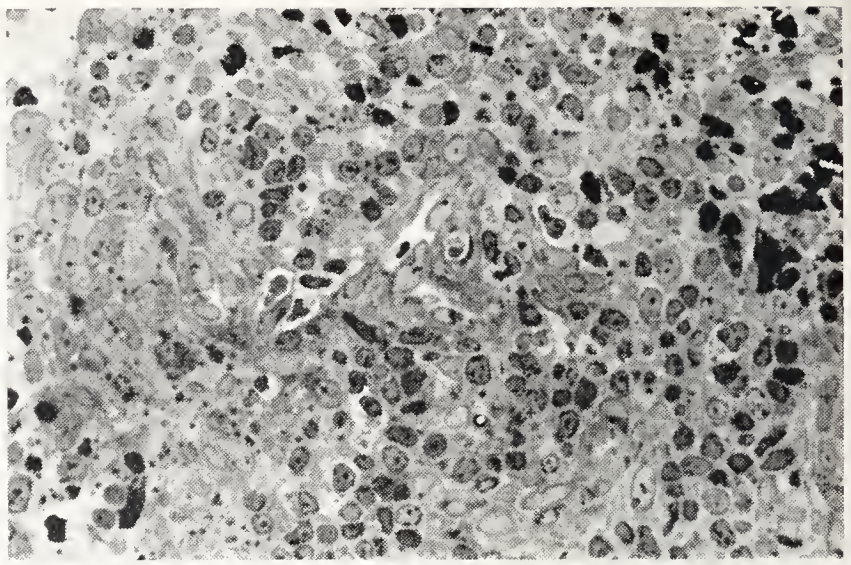

Figure 2. (X130X4.7) Spleen of a 27 old fetal rabbit showing in the main large pale reticular cells and only a scattering of the darker small lymphocytes. Most of the lymphocytes are perivascular suggesting recent arrival at the organ. (courtesy of Dr. H. Z. Movat).

While it was assumed in the past that the germinal centres of the spleen and lymph nodes were the major source of small lymphocytes, the data presented here points to the thymus as the major source. Sir Macfarlane Burnet[13] has recently discussed the possibility that the "first level" lymphocytes produced by the thymus are immunologically uncommitted, but where these cells lodge in suitable tissues such as lymph nodes and spleen, they have the possibility of becoming committed to specific antibody production when stimulated by an antigen. As Dameshek[14] points out, this is quite a reversal for Burnet, whose clonal selection hypothesis had indicated that at birth or shortly thereafter, all immunological competent cells were already committed to the production of single antibodies against single specific antigens. Thus, an antigen when it entered the body would wander about until it found its predestined specific clone of immunocompetent cells or immunocytes. (See *The Mechanism of Immunity* by Sir Macfarlane Burnet; Scientific American, January 1961)

But Burnet's recent work with a strain of New Zealand mice, having a genetically determined autoimmune hemolytic anemia led him, according to Dameshek, to modify his theories considerably. In studying these unusual mice Burnet found that (1) transmission of the disease to young mice of the same strain could be achieved with the injection of spleen cells, (2) the thymus of affected mice showed germinal centres and plasma cells (i.e. presumed antibody production), (3) thymectomy could prevent development of the hemolytic state.

Interpretation of these results led Burnet to his postulation of two 'levels' of lymphocytes — one in the thymus, the other elsewhere in lymphoid and splenic tissues. Although Burnet considers the thymic lymphocytes as uncommitted, under abnormal conditions, as in genetically determined auto-immune hemolytic anemia (and perhaps in other auto-immune disorders), 'forbidden' (committed) clones of abnormal lymphocytes might be present. When these clones react with normal body antigens, in the thymus or elsewhere, abnormal auto-antibodies could result. Therefore the thymus must be reckoned with in a cellular theory of immunity.

A *second theory* for the lymphocyte depletion in thymectomized animals is that the thymus may act as an endocrine organ and secrete a hormone which would stimulate lymphopoiesis. Recently Metcalf[15] has described a 'lymphocytosis stimulating factor' extractable from the medulla of the thymus and from no other organ, which, when injected intracerebrally into newborn mice, causes a blood lymphocytosis, maximum in about six days. This factor will maintain lymphocyte levels of thymectomized adult mice. The titre of lymphocytosis stimulating factor in the thymus is low at birth but rapidly increases to high levels. It is found in involuted thymus of elderly humans, a finding which suggests that the functionally active cells may be Hassall's corpuscle cells[15]. Tissue cultures of thymic fragments produce it; adrenal hormones suppress its production. But as Waksman[10] et al. point out, in contradiction to these observations, DNA lymphopoiesis as measured by P^{32} pickup during synthesis or by mitotic counts is not altered in lymph nodes following thymectomy. Failure of thymic homogenates to restore immunologic competence to the thymectomized rat or mouse would argue against any exclusively hormonal role for the thymus. On the other hand, restoration of homograft reactivity to thymectomized mice by transplantation of intact viable thymus suggesting as it does that the thymus is a direct source organ of small lymphocytes, does not exclude an ancillary hormonal function.

Possible Clinical Applications

Clinically, the status of the thymectomized animals invites comparison with human diseases in which there is a loss of immunologic function. In hypo — or agammaglobulinemia, a failure to make antibodies or to resist pyogenic infection is coupled with an absence of germinal centres and plasma cells from lymphoid organs and of gamma globulin from the serum. Blood lymphocyte levels and delayed reactive capacity are normal however. The thymectomized animal shows a closer resemblance to the less well studied human case of lymphopenia which occurs in association with agammaglobulinemia and in which there is a loss of resistence to various viral, fungal and chronic bacterial infections[10]. Infants with this disease are emaciated, suffer numerous infections, have lymphocytopenia in blood, and have marked lymphoid and splenic atrophy (similar to 'thymic cachexia'). This condition might therefore be based on congenital atrophy or disfunction of the thymus.

Summary and Commentary

Thus, in summary, the thymus appears to be the principle source of the small lymphocyte population of the blood, spleen and lymph nodes. It may in addition produce hormonal factors affecting lymphocyte production. It seems to play a major role early in life and perhaps later as well, in maintaining the immunologic integrity of the organism.

However, the physiological function of the thymus is far from being resolved. The experimental data of recent months leads to many questions. For example, Miller working with thymectomized mice found a disappearance of germinal centres and only a few plasma cells in the spleen and lymph nodes. Waksman, experimenting on rats, found these organs intact. Is this merely a species difference? Perhaps the rat is more immunologically mature at birth and therefore neonatal thymectomy does not alter pre-existing lymphoid structure. Yet this implies that the small lymphocytes are the precursors of other mononuclear cells — large lymphocytes and plasma cells. This is conjectural, for what is the criterion of a large and a small lymphocyte and how does one differentiate between them?

Another question concerns Metcalf's 'lymphoytosis stimulating factor' of the thymus. Is there any relationship between this hormone and Sainte-Marie and Leblond's lymphocyte, attracting factor in the thymic medulla; and in broader terms, does the lymphocytosis stimulating factor even exist?

A third area of debate questions Burnet's lymphocyte 'level' hypothesis. If, as he now claims, the thymus seeds the lymphoid tissues with immunologically uncommitted small lymphocytes, one wonders the mechanism by which these lymphocytes can become immunocompetent cells capable of reacting with antigens. In other words, do the small lymphocytes still differentiate in accordance with Burnet's clonal 'selective' theory? Or do they in fact differentiate in terms of the older mechanical 'instructive' theory which holds that the invading protein, or antigen, acts as a template

against which an antibody protein somehow moulds itself?

There are other questions of course, but these will only be answered by further experimentation on the thymus — no longer an organ of mystery.

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OBESITY *Continued from page 188*

of the belladona group have been used. None has any place in the treatment of obesity.

Conclusion

Since the time of Hippocrates, the dangers of obesity have been recognized and dietry therapy advocated. Unfortunately, many people still refuse to accept these facts and wait patiently for the development of a new and easy method of weight reduction. Henry S. Leigh wrote the following during the last century:

> If you wish to grow thinner, diminish your dinner,
> And take to light claret instead of pale ale;
> Look down with an utter contempt upon butter,
> And never touch bread till its toasted or stale.[7]

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Book Review

Correlative Neuroanatomy and Functional Neurology; J. G. Chusid and S. J. McDonald; Lange Medical Publications, Los Altos, California, Eleventh edition, 1962; 384 pages, illus., $5.50.

The nervous system is the most complex system of the body: a neurologist will proudly say that the other systems merely protect and maintain *his* system.

This 1962 edition, in the famous Lange series, touches briefly on many facets of present nervous system knowledge. The first section reviews brain, spinal cord, peripheral nerve and autonomic anatomy. Diagrams of nerve pathways add detail for photographic minds. Notations are brief, sometimes even cryptic, and reference where possible is made to clinical conditions. The middle section deals with neurodiagnosis. Motor and sensory functions and their tests are included as well as CSF studies and electrodiagnostic methods. The last section deals with CNS disorders. Although aiming at completeness, many brief references to certain conditions, especially the neuromuscular disorders, may leave one confused.

In summary, the book is useful primarily for students', but also for graduates' reviews. Especially helpful for 2nd meds students is the neurological examination in the appendix of the book. *J.D.G.*

Medical Horizons

A MONTH IN SPAIN

Last summer, I spent the month of June as an externe in La Gran Hospital de la Beneficia in the capital of Spain, Madrid. I will attempt to reflect upon my experiences — medical, cultural, and social.

It is very important to realize that Spain initially impresses one as being a very provincial country. It is in a sense isolated from the rest of Europe both physically by the Pyrinees and also politically by a twenty-year dictatorship, but most important to the Anglosaxon visitor, the people speak predominantly Spanish, French, German and English, in that order, are the other languages spoken.

The firm handshake of Doctor Juan Garcia Paredes, chief resident in medicine, dispelled all my fears and doubts. I was assigned to a large, clean, single room on the ninth floor of the hospital which provided a panoramic view of downtown Madrid. The hospital seemed to be comparable in size to the Wellesley Hospital; however, the nurses are quite different. Meal hours are several hours later than in Canada with supper finally being served between nine-thirty and ten-thirty at night.

I was obliged to report at nine-thirty each morning, Monday through to Saturday. There then would follow two hours of general rounds (in Spanish) with the chief of Medicine, a truly grand man in his field. After termination of rounds at eleven-thirty, there were usually heated discussions lasting from one to three hours regarding therapy. My exhausting day had thus ended by 1:00 p.m. By the time that I had served twenty days of this service, guilt feelings were quickly mounting, but within the next few days, I had several doctors congratulate me for being the most attentive foreign student in years!

There were many interesting and amusing incidents during my stay. On the second day, I was introduced to the nun who was the chief nurse of the floor. She gave me quite a warm smile, spoke something in Spanish and then with a perplexed expression turned to the doctor for further conversation. The doctor returned crimson with embarrassment and stopped me with the leading question, "What religion are you?" With my rudimentary Spanish, I leaped forward "Yo soy agnostico" (I am an agnostic). As the expression of disbelief spread across the sister's face, I thought that surely lightning would strike, however, forthrightedness paid off and we became fast friends.

One evening, there was a very special occasion. A patient, low in funds I suppose, paid for medical services with a side of beef. The beef was specially cooked, extra wine was bought, and everyone turned out in fine spirits. The meal itself was superb. Following this, the tables were cleared and guitars brought out. The singing and high jinks that followed were most moving, humorous and most likely typical of such an environment anywhere.

Madrid is a most interesting city. Although structurally not as old as neighbouring cities and villages, it is indeed rich in tradition and art. The Prado Museum contains some of the world's most well known paintings. The colourful night life starts late and correspondingly ends late. The Royal Palace stands in all its glittering splendour perhaps awaiting Juan Carlos Bullfights on Thursday and Sunday afternoons which are exciting spectacles. About Madrid are the intriguing areas of Toledo, El Escorial, La Granja, and Segovia.

There is quite an impressive respect for teaching facilities and graduates from the University of Toronto. Dr. Castro, no relation, whom I observed doing open cardiac surgery, did post-graduate work at Toronto General Hospital with Dr. Bigelow. Many Canadian texts rest upon the Spanish students' shelves. In conclusion, I wish to assert that summer externeship in Spain is definitely lacking in scope of experience; however, culturally, I do not believe that there is any other country in Europe more worthy of an extended visit.

Wm. S. Crysdale 6T4

Abstract –

Adrenal Steroids and The Pattern of Metastases of Breast Cancer; Jama; 28 July, 62; Vol. 181, no. 4.

Adrenal steroids have been used for about 10 years in the treatment of disseminated carcinoma of the breast. This is a study of 20 patients. Patients receiving additive adrenal steroid therapy had a significant increase in metastases to the lungs, liver, and heart, and also to the opposite breast and especially to the mucosa and submucosa of the gastro duodenum, brain and spleen. The therapy seems to decrease the host resistance to the cancer by decreasing antibody formation. The permeability of both lymphatics and blood vessels may also be increased. Yet the overall survival rate was about the same as that of the control.

F.L.

Answers to On Inspection

Questions — page 190

FIGURE 1: Glossitis.

This picture may present in vitamin deficiencies (ariboflavinosis, pellagra), pernicious anemia, iron deficiency anemia, sprue and other malabsorbtion syndromes.

A deficiency of riboflavin (vitamin B_2) results in a syndrome (ariboflavinosis) of angular oral fissures, corneal vascularization, photophobia, skin and lingual changes. The tongue may take on a so-called magenta hue, strongly resembling the red-blue coloration of cyanosis, because of atrophy of the lingual mucosa; it may also become fissured longitudinally.

Pellagra is a syndrome due to a deficiency of nicotinic acid, and is characterized by dermatitis, glossitis, stomatitis, diarrhea and dementia. The lingual changes consist essentially of vascular congestion and edema, and atrophy of the mucous membrane and ulceration so that the tongue becomes red, swollen and beefy.

The lingual changes of pernicious anemia and iron deficiency anemia are familiar to all. The glossitis of the malabsorption syndrome is due to multi-nutritional deficiencies, and does not present a characteristic picture.

FIGURE 2: Stomatitis.

Stomatitis, inflamation of the mucous membrane of the mouth, may be catarrhal, suppurative, follicular, papular, vesicular, pustular or gangrenous in nature. It may be due to a multitude of causes which include vitamin deficiencies (see 1), drug intoxications, trauma, and specific viral, parasitic and bacterial infections.

FIGURE 3: Necrobiosis Lipoidica Diabeticorum.

This disorder, the etiology of which is not known, is characterized by lesions which begin as small papules usually on the legs at the sites of trauma, which gradually enlarge to become large plaques occasionally covering the whole surface of the lower leg. Ulcers are not uncommon. Pathologically, glycogen is found in the lesions, not only in the histiocytes but in the tissue spaces as well. Of all people who develop these lesions, 90% are, or are going to become diabetic.

FIGURE 4: Pellagra. (see also 1, 2)

Pellagra (nicotinic acid deficiency) is a seasonal disease, the incidence of which parallels remarkably the seasonal variation in the intensity of sunlight; the reason for this is not known. It is known that corn has a pellagragenic activity because of its low nicotinic acid content, and, just as important, its low levels of tryptophane, the amino acid precursor of nicotinic acid. In summary then, pellagra may be thought of as the syndrome which results from exposure to the sun of the person depleted of nicotinic acid and protein (tryptophane).

The charateristic skin changes consist of symmetrical, well-demarcated, hyperkeratotic, scaling lesions on the exposed surfaces — wrists, hands, tops of feet, face. Later desquamation of the epidermis occurs resulting in a variegated dermatitis, with brown scaly areas, alternating with areas of depigmented, shiny, atrophic skin.

FIGURE 5: Obesity.

Obesity occurs when the caloric intake exceeds the energy requirements of the body, both for physical activity and for growth. As a result, there is an accumulation of fat which is stored in the adipose tissue. The excess deposition of fat is associated with an increased tendency to the development of the serious degenerative diseases such as atherosclerosis, diabetes, degenerative arthritis, hypertension and even cancer. The only common cause of death which does not strike earlier in the obese than in the lean population is suicide. The only effective treatment for obesity is the restriction of caloric intake below the energy requirement.

FIGURE 6: Anorexia Nervosa.

Anorexia nervosa, or psychogenic undernutrition is seen in emotionally disturbed patients, usually young adult females. There is frequently a story of some sort of sexual difficulty, and strangely enough, although there is almost complete disappearance of the normal fat depots, there is no atrophy of the breasts. These individuals usually have a history of having previously been slightly overnourished. In an attempt to return their body to a level they consider esthetic, they restrict calories only to discover after a few weeks that they are unable to eat and consequently cannot stop their weight reduction. Treatment consists essentially of persuading the patient to eat.

S. M. Zweig 6T3

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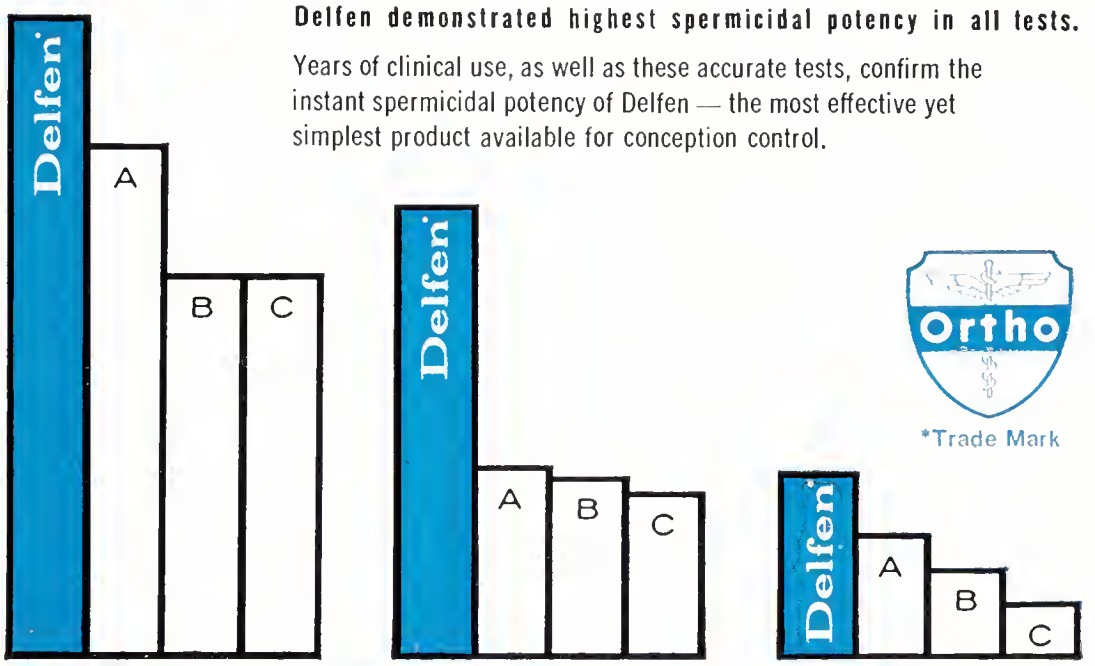

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Reference: (1) MacLeod, J.; Sobrero, A., and Inglis, W.: In Vitro Assessment of Commercial Contraceptive Jellies and Creams, J.A.M.A. **176**:427-431 (May 6) 1961.

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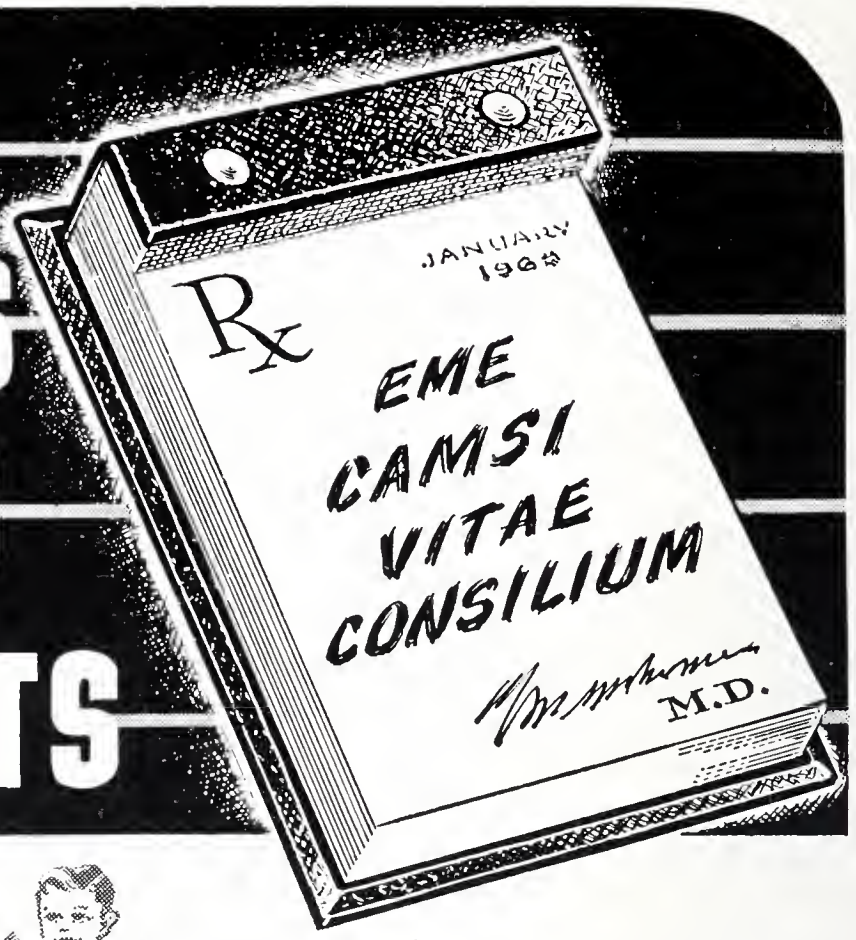

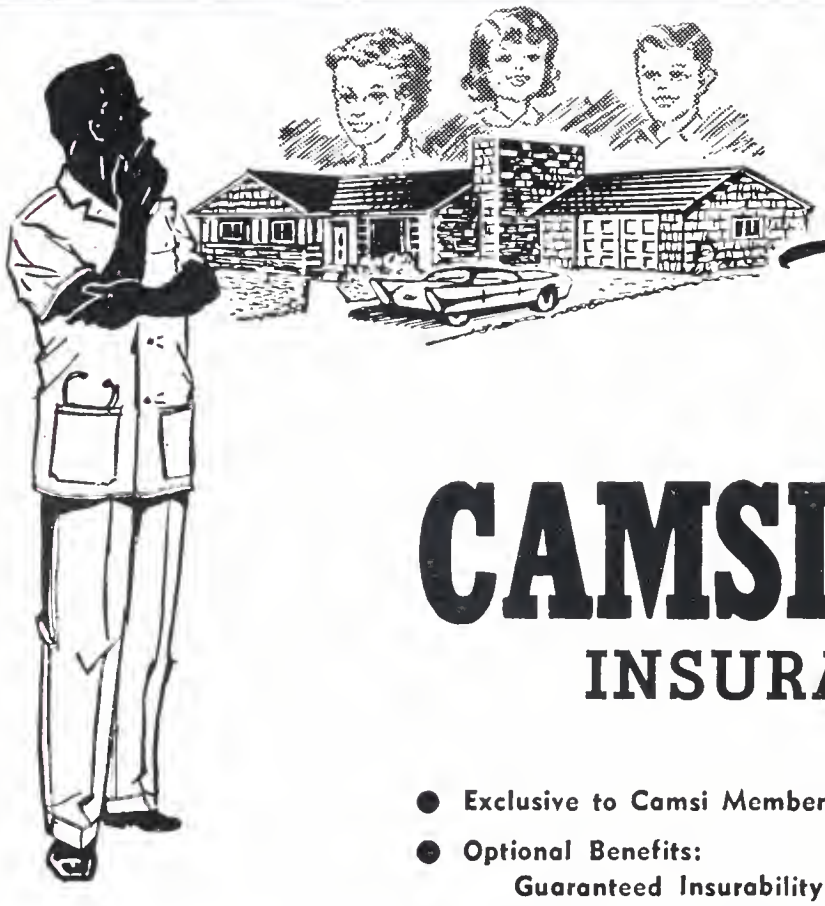

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